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ROLE OF THE ADRENAL CORTEX IN DISEASE.[1]

By KEITH HARRISON,
Royal Prince Alfred Hospital, Sydney.

OUR knowledge regarding the adrenal cortex has advanced immeasurably since Thomas Addison, that somewhat dour and forbidding Guy's Hospital physician, first attributed the causation of a rare malady to a disorder of the suprarenal capsules. It has advanced owing to the efforts of many notable investigators, and these efforts have been redoubled since the therapeutic value of the adrenal steroids has been made evident in so many fields of medicine.

I will endeavour to deal briefly with the disturbed physiological and metabolic processes that are met with in disorders due to deficiency or excess of adrenal secretion, and to indicate the part played by the adrenal glands in the response of the body to stress. No attempt will be made to discuss detailed diagnostic measures or the use of the adrenal steroids in therapy.

Physiological Actions of the Adrenal Cortical Hormone.

Information regarding the actions of the adrenal cortical hormone can be obtained from a study of adrenalectomized animals or of patients suffering from Addison's disease, or, conversely, from observing the effects of administration of the potent adrenal steroids.

Mineral Metabolism.

Adrenal cortical hormone influences the renal tubule to absorb sodium and chloride from the fluid passing through it. If this hormone is lacking, the output of sodium and chloride may continue at an excessive rate even after the plasma concentration has fallen well below the normal threshold level. This immoderate excretion of sodium and chloride depletes the plasma and the extracellular tissue fluids. Potassium ion passes out from inside the cells to maintain ionic equilibrium, so that its concentration tends to rise in extracellular fluids and in the plasma. There may, in addition, be some specific retention of potassium by the renal tubules.

It is important to realize that when adrenal cortical hormone is deficient, the renal tubules not only are unable to reabsorb sodium efficiently when the concentration in the tubular fluid is low, but also are inefficient in excreting sodium in excess when the concentration in the tubule is high. That is, there is lessened flexibility of the renal tubule in the regulation of electrolyte excretion. Hence the Addisonian patient is less able to cope with an excessive administration of salt, especially when given intravenously, than the normal individual, and may quite easily perish from pulmonary œdema due to over-enthusiastic therapy with saline. Excessive retention of sodium may be noted when cortical steroids are administered in excess. This is particularly the case with desoxycorticosterone, but may be seen in some patients given cortisone or ACTH. Associated with the retention of sodium there may be excessive excretion of potassium and chloride, with a corresponding fall in the plasma levels. Hence it is considered (Thorn *et alii*, 1950) that the use of mercurial diuretics is contraindicated when patients are under intensive treatment with cortisone or ACTH, as the resulting potassium diuresis may cause dangerous tissue depletion. This can be prevented by adequate potassium dosage during treatment.

Water Metabolism.

In general, water tends to follow the excretion of sodium and chloride, so that concentration of the plasma and tissue dehydration are pronounced features of the Addisonian crisis. However, the renal tubule of the

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on July 26, 1951.

adrenalectomized animal lacks flexibility in the excretion of water too, so that there is a poor diuretic response to the ingestion of a large test dose of water. This phenomenon is utilized in the test for adrenal insufficiency described by Robinson, Power and Kepler (Levy *et alii*, 1946). Desoxycorticosterone does not correct this abnormal test response, whereas cortisone in adequate doses may restore the function to normal. Patients with Addison's disease have been shown to have abnormally high levels of pituitary antidiuretic hormone in blood and urine (Thorn *et alii*, 1951), so that this may be one of the mechanisms, at least, by which water diuresis is inhibited. Overdosage with adrenal steroids may cause undue retention of water with sodium, leading to overhydration and œdema.

Acid-Base Balance.

The concentration of bicarbonate in the plasma is usually not altered in adrenal insufficiency, but the level may rise under the influence of excessive cortical steroid. It is due to the fall in extracellular chloride and potassium that has been previously noted. Thus hypokalæmic hypochloræmic alkalosis has been described in Cushing's syndrome and after therapeutic administration of cortisone and ACTH, and it will respond to potassium and chloride therapy.

Carbohydrate Metabolism.

Patients with adrenocortical insufficiency are liable to develop hypoglycæmia and are exceedingly sensitive to insulin. Several cases have been described in which adrenal insufficiency has developed in patients with established *diabetes mellitus*. This has caused a remarkable fall in the insulin requirements of these patients and has confirmed clinically the earlier observations of Long that adrenalectomy ameliorates pancreatic diabetes in dogs. A fascinating case report (Green *et alii*, 1950) describes the effect of total adrenalectomy on a woman, aged twenty-eight years, suffering from severe diabetes and malignant hypertension. After a stormy and tedious post-operative period she attained a state of relative though delicate stability, in which her hypertensive signs were found to have regressed, and the control of her diabetic condition required much less insulin. The amount of insulin eventually required was roughly proportional to the amount of cortical extract given, though it was uninfluenced by the administration of DOCA. Incidentally, the blood pressure level was readily elevated by DOCA, less readily by aqueous cortical extract, and not at all by lipo-adrenal cortical extract.

Administration of cortisone or ACTH to animals regularly produces a diabetic state, and a temporary diabetic syndrome has been produced in some normal individuals by the use of ACTH. However, when the non-diabetic patient is given large doses of cortical steroid, he is usually able to control the hyperglycæmic tendency by an extra secretion of insulin. It is suggested that the few patients who respond by the development of a frank diabetic state are those with a low pancreatic islet reserve.

Cortical hormone appears to influence carbohydrate metabolism by promoting gluconeogenesis from protein and by impairing the peripheral oxidation of glucose. In a recent review of this subject (Engel, 1951), it is stated that the liver glycogen levels of adrenalectomized animals decline rapidly on fasting in contrast to those of normal animals, which fall more slowly under the same circumstances. The major defect in gluconeogenesis appears to be related to the difficulty in mobilizing endogenous protein for catabolism. Adrenalectomized animals can be maintained in good condition without hypoglycæmia on protein-rich carbohydrate-free diets, so that they must be able to form carbohydrate from dietary amino acids. In fact, injected amino acids appear to be converted to urea in the adrenalectomized-nephrectomized rat as efficiently as in the normal animal.

The fractions of the adrenal steroids that have an active influence on carbohydrate metabolism are those with an oxygen atom at the "11" position in the nucleus. Desoxycorticosterone is inactive in this respect.

Nitrogen Metabolism.

After administration of cortisone there is increased excretion of nitrogen in the urine, owing to increased protein breakdown. Similar findings are noted in Cushing's syndrome, in which the muscular weakness is probably due partly to loss of muscle protein.

A striking result after the administration of ACTH is the pronounced increase in the urinary excretion of uric acid, mainly owing to a change in the renal clearance of uric acid.

Hæmopoietic System.

Lymphatic Tissue and Lymphocytes.—In Addison's disease there are commonly an increase in the size of the lymphatic structures and peripheral lymphocytosis. After administration of adrenal steroids lymphoid tissue disintegrates and the number of circulating lymphocytes usually falls.

Eosinophile Cells.—Even more striking and consistent than the fall in lymphocytes is the fall in the number of circulating eosinophile cells which regularly occurs after adequate doses of cortical hormone.

Neutrophile Cells.—Administration of cortical hormone usually causes mild neutrophile leucocytosis. In conditions associated with neutropenia, such as disseminated *lupus erythematosus*, treatment with cortisone commonly produces a rise in the neutrophile cell count.

Erythrocytes.—Cortisone produces reticulocytosis when given in certain disorders and may inhibit some hæmolytic processes. Polycythæmia is a feature of Cushing's syndrome, but has not yet been unequivocally reproduced by administration of steroid hormones.

Immune Reactions.

It has been suggested that there was an increase in circulating antibodies after administration of cortical hormone, owing to dissolution of lymphoid tissue with release of the globulin antibodies contained therein. This has not yet been adequately confirmed. Adrenalectomized animals are more vulnerable to anaphylactic reactions than normal animals. Adrenal steroids have been found clinically useful in several conditions that are considered to have an allergic basis. It is probable that adrenal steroids alter the allergic tissue reaction that follows the union of antigen and antibody, but they do not prevent the local or general reactions to histamine as such (Thorn *et alii*, 1950).

Neurological Phenomena.

Muscular weakness, ready fatigability and emotional irritability are found in many patients with Addison's disease. A high proportion of such patients, too, have an abnormal electroencephalogram with a characteristic slowing of the α rhythm. The restoration of this rhythm to normal requires a relatively large amount of cortisone; DOCA is not effective.

A proportion of patients treated with adrenal steroids in large doses exhibit euphoria which may even progress to a frank psychosis.

Adrenal Cortical Steroids.

Though over 30 steroids have been fractionated from the adrenal cortex, and the amorphous fraction left behind is still very potent, they may be arranged in four groups from the functional point of view. Many of the isolated steroids are physiologically inactive.

Mineralo-Corticoids.

The mineralo-corticoids are exemplified particularly by desoxycorticosterone. These efficiently counteract, in low dosage, the electrolyte abnormalities of adrenalectomized animals, and in higher dosage may cause undue salt and water retention and loss of potassium. Desoxycorticosterone has been isolated from the adrenal gland, but it is not known whether it is a normal product of the gland. It can be synthesized, is relatively cheap, and is of immense value in the practical management of patients with Addison's disease.

Gluco-Corticoids.

Several of the isolated steroids exert a potent influence over carbohydrate metabolism, the most active being Kendall's compound E, or 11-dehydro-17-hydroxycorticosterone, or cortisone, and Kendall's compound F, or 17-hydroxycorticosterone.

In addition to their carbohydrate-regulating action these steroids have a wide influence on metabolic processes, as was indicated previously. Cortisone has approximately one-fiftieth the electrolyte-regulating activity of desoxycorticosterone—that is, one milligramme of DOCA is equivalent to 50 milligrammes of cortisone in this respect. These steroids are partly utilized or destroyed in the body and a small fraction is excreted as corticoids in the urine, in which they can be estimated biologically or chemically.

Androgenic Steroids.

Several steroids with an androgenic action have been isolated from the adrenal cortex, though testosterone itself does not seem to have been obtained from there. These steroids are largely excreted in the urine as inactive 17-ketosteroids, which can be estimated colorimetrically with relative ease.

Œstrogens and Progesterones.

Steroids with œstrogenic and progestational activity have been isolated from the adrenal cortex, and a few cases have been reported of feminizing adrenal cortical tumours in which there was evidence of production of a great excess of œstrogenic material.

Does the adrenal cortex normally secrete several chemically different steroids, perhaps in response to differing physiological requirements? Are there two distinct cortical hormones—mineralo-corticoid and gluco-corticoid? Or can all the activities of the adrenal cortical secretion be explained by the existence of one steroid alone? These questions cannot yet be answered, but some relevant points may be considered.

It would appear that in certain pathological conditions associated with hyperplasia or tumour of the adrenal cortex, excess androgenic steroid can be produced, sometimes at the expense of the life-maintaining corticoids, as in the infantile adreno-genital syndrome. It has been shown, too (Bartter *et alii*, 1951) that administration of ACTH to female patients with the adreno-genital syndrome increased the output of 17-ketosteroids, but produced none of its other usual metabolic effects. Administration of cortisone produced a fall to normal in the elevated urinary 17-ketosteroid excretion.

However, these disorders are probably best considered as rare aberrations of cortical hormone secretion, and they do not prove that a separate androgenic steroid is normally secreted from the adrenal cortex. The normal level of excretion of 17-ketosteroids may possibly come from degradation of non-androgenic steroid elsewhere in the body. It has been shown (Sprague *et alii*, 1950) that almost all the clinical and laboratory manifestations of spontaneous Cushing's syndrome have been reproduced in normal individuals by the administration of cortisone alone. These manifestations include acne and hirsutism, which are considered androgenic phenomena, and œdema, hypertension, sodium retention and potassium loss, which may be attributed to mineralo-corticoid activity. Sprague *et alii* cautiously conclude that a sufficient number of the features of Cushing's syndrome have now been induced by cortisone alone to warrant the suspicion that a cortisone-like steroid may be the principal, if not the only, hormone responsible for the production of the syndrome.

As final proof of the role played by cortisone in the production of this syndrome it would be interesting to know if these phenomena have been reproduced in an Addisonian patient by cortisone. One would suspect that the patient deficient in endogenous cortical secretion would respond even more sensitively than normal to exogenous hormone treatment. Similar results have been obtained in the normal individual with prolonged dosage with ACTH. As the manifestations of cortisone and ACTH overdosage are extremely similar, it would seem probable that ACTH stimulates the secretion of one adrenal steroid alone.

Selye (1951) has postulated that gluco-corticoid secretion is controlled by ACTH and mineralo-corticoid secretion by somatotrophin—that is, pituitary growth hormone. The experimental basis for this assumption has not been adequately confirmed by other workers.

Biological assay of cortical hormone in blood from the adrenal vein has been attempted on several occasions. A recent report (Paschkis *et alii*, 1950) describes the estimation of adrenal cortical hormone levels in adrenal vein blood obtained from trained, unanæsthetized dogs, by means of the liver glycogen assay method of Venning. Expressed as microgramme-equivalents of compound A, levels of the order 14 to 20 units were obtained. Small increases above these levels were found after administration of ACTH and adrenaline. In the arterial plasma they obtained levels of 11 to 12 microgramme-equivalents, a finding which seems unduly high in comparison with that obtained from the adrenal vein. Though these results were expressed in units, compound A being used as the standard, Paschkis *et alii* make no suggestion that compound A was the actual substance responsible for the glycogenic activity.

There is some evidence (Nelson *et alii*, 1950) that the steroid present in the adrenal vein blood of dogs is 17-hydroxycorticosterone, or compound F. Fundamentally, we want to know whether there is an enzyme system or group of systems in the tissues on which the cortical hormone acts, and whether inhibition or acceleration of one type of enzymic reaction can explain its multifarious activities.

Adrenal Insufficiency.

The features of adrenal insufficiency are classically witnessed in the adrenalectomized dog or in the patient whose adrenal glands have been destroyed by disease. Deficiency of adrenal secretion and atrophy of the glands accompany the general endocrine atrophy in hypopituitarism. These features are seen, too, in the infant suffering from the adreno-genital syndrome, whose adrenal glands seem to be manufacturing androgens at the expense of the life-saving corticoids. Finally, attention is being directed to the possibility of relative adrenal insufficiency in debilitating and stressing medical and surgical disorders.

Addison's Disease.

The patient with Addison's disease presents usually with a history of insidious onset of fatigability, irritability, digestive disturbances, weight loss, and pigmentation of the skin. Dr. W. A. Bye (personal communication), after reviewing the case records of the Royal Prince Alfred Hospital, has stressed the frequency of abdominal discomfort as the initial symptom in this disorder—a symptom that was almost invariably misinterpreted until more definite signs appeared. The slow course of the illness may be punctuated by acute exacerbations, commonly precipitated by infection or injury. In these crises the picture resembles that seen in the adrenalectomized dog: weakness increases to the point of collapse, vomiting occurs, the blood pressure falls further, renal secretion ceases, and death commonly occurs from peripheral circulatory failure.

During the steady course of the illness the electrolytes in the blood may be altered little if at all. During a crisis the plasma sodium and chloride levels fall, the potassium level rises, and the blood urea may attain uræmic levels.

The condition of the patient with Addison's disease may be moderately improved by the prescription of a high salt intake, further benefited by administration of desoxycorticosterone acetate, and restored nearly to normal by the addition of cortisone to this régime. However, at best, his resistance to stress will be distinctly impaired; infections and surgical procedures will be withstood with some difficulty, and he will be unduly sensitive to toxins and to certain drugs, such as morphine.

Hypopituitarism.

Deficient adrenal secretion is part of the overall endocrine deficiency seen when pituitary stimulation is lacking. The patient suffering from Simmonds's syndrome may manifest clinical signs of adrenal insufficiency, but usually this is latent until stress is encountered or until metabolism is stimulated by administration of thyreoid hormone. It is well recognized that incautious treatment of patients suffering from pituitary myxœdema with thyreoid extract may readily precipitate a crisis of adrenal insufficiency. It would appear that the depressed secretion of cortical hormone is just sufficient for the tissue requirements at a low level of metabolism, but is insufficient when these requirements are raised by thyreoid hormone replacement.

Adrenal Insufficiency in the Adreno-Genital Syndrome.

A few cases have been reported (Wilkins, 1949) of pseudohermaphroditic infants suffering from the adreno-genital syndrome due to adreno-cortical hyperplasia, who have shown signs of adrenal insufficiency. The symptoms have included vomiting, weight loss, dehydration and collapse, and they have responded to therapy with salt and desoxycorticosterone. Treatment with cortisone has been shown to suppress the excessive excretion of 17-keto-steroids and of biologically active androgen.

Relative Adrenal Insufficiency.

The concept of relative adrenal insufficiency assumes that under certain conditions of stress the output of cortical hormone may be insufficient for the increased requirements of the body and that prolonged overstimulation of the glands in response to traumatic or debilitating illness may lead to exhaustion of the cortex. It would seem desirable to find out whether such cortical exhaustion had occurred by some procedure such as the response of the circulating eosinophile cells to a test dose of ACTH. If the response was inadequate, a fillip from ACTH or replacement with cortisone might enable the patient to resist an episode such as an operation. Such a test by the use of ACTH or adrenaline may well become a part of the routine pre-operative investigation of potentially exhausted patients.

Adrenocortical Hyperactivity.

Cushing's Syndrome.

Originally described by Harvey Cushing as being due to a basophile pituitary adenoma, it is not now doubted that the clinical manifestations of Cushing's syndrome are due to excessive production of one or more steroid hormones by hyperfunctioning adrenal cortices (Sprague *et alii*, 1950). Almost all the features of the syndrome have been reproduced by therapeutic overdosage with ACTH and cortisone.

The exact relationship that the basophile adenomata or the hyaline changes of Crooke bear to the hyperactive adrenal cortex is not yet clear. It has been assumed that the basophile cells secrete an excessive amount of ACTH, which initiates and maintains the process. A recent case report (McCormick *et alii*, 1951) describes a patient suffering from coexisting acromegaly and Cushing's syndrome, in whom an eosinophile adenoma of the pituitary gland was demonstrated at operation and at autopsy, and in whose circulating blood increased levels of ACTH were said to have been demonstrated. These authors postulated that the excessive secretion of ACTH had been produced by the eosinophile cells.

A further report (Bornstein and Trewhella, 1950) gives additional evidence that there is an increased output of ACTH in some cases of Cushing's syndrome. These authors estimated the content of ACTH in the peripheral blood, using Sayer's method in the hypophysectomized rat. Normal controls averaged 197 microgrammes of ACTH-like activity per 100 mils of plasma, whereas three patients with Cushing's syndrome averaged 451 microgrammes of ACTH-like activity per 100 mils of plasma. On the other hand, it would seem evident that in those cases of Cushing's syndrome in which there is a true hyperfunctioning adrenal cortical tumour, there is severe depression of ACTH secretion by the pituitary, as in these patients the opposite adrenal gland is found to be greatly atrophied. Such patients are particularly likely to suffer from an adreno-cortical crisis when the tumour is surgically removed. Adult patients with the adreno-genital syndrome due to a cortical tumour withstand surgical removal of the tumour relatively much better. True cortical hormone in excess depresses pituitary secretion of ACTH; excess circulating androgen depresses it little if at all.

Adreno-Genital Syndrome.

The adreno-genital syndrome may begin antenatally, so that a female baby may be born as a pseudohermaphrodite or it may commence later in life, when female patients will exhibit the features of virilism. The occurrence of the syndrome in males is very rare and may cause one form of precocious puberty in boys. The manifestations are due to hypersecretion of androgen by the adrenal cortex, either from hyperplasia of the cells or from tumour.

Congenital adrenal hyperplasia causes pseudohermaphroditism in females and *macrogenitosoma præcox* in males. It is characterized by accelerated growth and muscular development, early growth of sexual hair, and progressive virilization.

In adult virilization the excessive secretion of androgen developing in the mature female gives rise to a masculine configuration and voice, hirsutism, genital atrophy with hypertrophy of the clitoris, and amenorrhœa. It is important to stress the significance of amenorrhœa as an early and constant symptom in this condition. Hirsute women who menstruate regularly will very rarely be found to be suffering from true adrenal hyperactivity.

The excretion of 17-ketosteroids, as well as of biologically active androgen, is moderately increased in patients with cortical hyperplasia and may attain colossal levels in those with a cortical tumour.

Response of the Adrenal Cortex to Stress.

It has long been realized that the adrenal cortex hypertrophies in response to varied stimuli applied to the animal body, and that an increased urinary excretion of corticoids follows injury, burns, exposure to cold, and so on. These responses do not occur in the adrenalectomized or hypophysectomized animal, so it would appear that such stimuli act on the adrenal cortex by means of ACTH from the anterior lobe of the pituitary gland. The stimulus to the pituitary cells may travel from the hypothalamus or it may be produced by circulating adrenaline from the adrenal medulla.

It would appear highly probable that this increased secretion of cortical hormone is beneficial to the animal and aids the bodily defences against the noxious agent.

The subject of the relationship of the adrenal glands to stress has received tremendous publicity in recent years from the writings of Hans Selye and from the possible connexion between this problem and the therapeutic efficacy of cortisone and ACTH. In considering the publications of Selye, it is important to attempt to sort out (i) the fairly well-established and confirmed experimental facts, (ii) the doubtfully controlled and unconfirmed experimental results in animals, (iii) the theories attempting to explain both these groups of results, and (iv) the highly imaginative, though very stimulating, application of these theories to disease processes in man.

1. There is little doubt that the general adaptation syndrome (Selye, 1946), with its alarm reaction, stage of reaction and stage of exhaustion, accurately represents the response of some animal species to a variety of noxious agents, such as prolonged cold, burns, extreme muscular exercise, or the injection of formaldehyde. The course and duration of the adaptation syndrome are greatly altered by adrenalectomy or hypophysectomy.

During the course of subjecting rats to prolonged stress, some were found to develop swollen, painful joints which resembled both grossly and microscopically the joint lesions of rheumatoid arthritis in man. These lesions

could also be produced by heavy overdosage with DOCA. In each case the lesions could be produced more readily if the joints were traumatized by injections of formaldehyde, insufficient to cause arthritis in normal animals. These joint lesions were prevented by prior administration of cortisone. Again it was found that some rats similarly subjected to stress or large amounts of DOCA would develop hypertension and nephrosclerosis if they were previously "sensitized" by unilateral nephrectomy and a high dietary intake of salt and protein. Again, other rats so treated might develop granulomatous lesions in the myocardium, similar in some ways to Aschoff nodes, or inflammatory reactions around arteries similar to *periarteritis nodosa.*

2. Similar results are held to have been produced by the use of a crude lyophilized anterior pituitary preparation instead of DOCA. More recently (Selye, 1951), by the use of a very small series of rats, it has been held that purified growth hormone will produce similar pathological lesions in "sensitized" animals.

3. The theory is propounded that DOCA acts directly on the kidney to produce excess renal pressor substance, and this in turn causes hypertension and necrotizing arterial lesions. Growth hormone, or somatotrophin, stimulates secretion of mineralo-corticoid and may have a direct tissue action as well. Stress causes the pituitary gland to secrete relatively more somatotrophin than ACTH, so that there is an unbalanced production of mineralo-corticoid and gluco-corticoid. Administration of cortisone or ACTH restores the normal proportion of the two corticoids.

These theories do not fit in with the findings of many other workers and will require much more critical confirmation before they can be generally accepted.

4. Finally, Selye has taken the tremendous step (Selye, 1950) of identifying the vascular and granulomatous lesions which he has produced in rats with apparently similar disease processes in man, such as arthritis, nephritis, hypertension, gout and *periarteritis nodosa.* It is important to remember that there is not a shred of human experimental evidence to support this concept. The only common link at present is that both groups of conditions are prevented or alleviated by ACTH and cortisone.

Hans Selye may be right. These diseases, and others, may be truly diseases of adaptation, and in the future we may indeed need to train specialists in stress and adaptation; but for the present I would agree with George Perera (1949), who has said: "We must regard the concept of the diseases of adaptation as interesting but highly speculative."

Summary.

1. The action of adrenal cortical hormone on the metabolic functions of the body is discussed.

2. The multiple activities of the isolated adrenal steroids are indicated, and the suggestion is advanced that these activities may be produced in the body by one steroid alone.

3. Adrenal insufficiency is considered from the point of view of primary, secondary and relative deficiency of cortical hormone.

4. The two main clinical aspects of adrenal cortical hyperactivity — namely, the adreno-genital syndrome and Cushing's syndrome—are briefly reviewed.

5. Reference is made to the manner in which the adrenal cortex responds to stress, and a brief critical evaluation of the general adaptation syndrome of Selye is attempted.

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EMOTIONAL FACTORS IN ALLERGY.[1]

By DAVID ROSS,
Sydney.

NEAR the turn of the century Charles Richet made his splendid contribution to medical knowledge when he sought to explain increased sensitivity of the organism to toxins on the basis of anaphylaxis, meaning "without protection". Hard on this followed von Pirquet, who first introduced the term allergy, or altered reaction. After some more or less acrimonious debate the latter term was endorsed to describe a variety of symptoms which have been classified as the allergic diseases.

The dramatic symptoms associated with these diseases have intrigued physicians for very many years, and much has been written on the subject. Great advances have been made, especially in the realm of therapy; but it is certain that we have no absolute understanding of the actual processes involved in the production of these symptoms, although I think that at long last we may be getting nearer to the truth. So prevalent are these disorders that it became incumbent on a number of physicians to devote their whole professional lives to the care of such patients. These, then, are the allergists of modern medical practice who have contributed so much to our understanding.

As far back as 1698 one John Floyer wrote: "The passion of Anger makes the Spirits restless and apt to produce the Fit of Asthma." Throughout the ages others have confirmed the truth of this observation, which happily has served to arouse the interest of those who practise psychological medicine. Not a few psychiatrists have contributed much towrads our present knowledge. Not unnaturally perhaps, the writings of the allergists and psychiatrists have tended to stress the importance of their own particular approach, and in this fashion the outmoded "either-or" concept of disease has tended to flourish in the field of allergy.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on May 31, 1951.

However, those of us who are interested in the psychosomatic approach are ready and willing to acknowledge the debt we owe to both as we strive to determine the role each of these factors is playing in the patient's ill health. It follows, then, that each case must be treated on its own merits. Each patient presents us with a different problem. In some, allergic factors are predominant without any real disturbance of the psyche; in others the reverse obtains; while in a very large number both factors seem to be of significance. If, then, a patient suffering from an allergic disorder—I think I prefer that term to allergic disease—is to receive adequate treatment, due regard must be paid to possible psychogenic factors, albeit they are of major or minor importance in the initiation or maintenance of his invalidity. Unfortunately, psychiatrists are in short supply and the demand is great, so that the majority of sufferers have been denied their expert assistance. Nevertheless, there is much that can be accomplishd by the average physician, provided only that he is prepared to devote a little time and care to these people.

After working for some years in the clinic at the Royal Prince Alfred Hospital, where perhaps a thousand cases are investigated from an allergic point of view each year, I came to realize that the results of treatment, while satisfactory up to a point, could hardly be regarded with equanimity. In a survey which I concluded recently amongst patients who had been under treatment for not less than three months, 67% expressed themselves as "a lot better", 27% were "a little better", and 6% were no better or worse. In assessing the significance of these figures, it must be taken into account that a specific allergen or allergens had been determined as a result of the history and skin sensitivity tests. A number of patients suffering from probable allergic disorders had been rejected when no specific allergen could be elicited. Nor were the satisfied group entirely free from manifestations of allergy. So we see that an appreciable number failed to benefit when treatment was conducted along lines which I venture to suggest were in accordance with the best principles of allergic practice. Something was missing, and I think it probably was a failure to recognize the importance of psychogenic factors in allergic disease, which brings me to the problem in front of us at this moment.

The nature of this problem was stated by C. H. Rogerson of London in these words:

> It is important to know whether any special personality features are common to many of these cases. Secondly, what is the significance of such personality features, if any; are they merely secondary to over-protection and other environmental difficulties found in such cases? Or can they be considered to be to some extent primary features of the individuals' endowment. If this is true they may be one part of the allergic constitution which has so often been postulated, and lastly, what relationship have these findings to the actual allergic attacks?

In a thoughtful paper Rogerson seemed to recognize the existence of an actual allergic personality. He suggested that these people had certain in-born, over-anxious, aggressive and dominating characteristics, which at an early stage in emotional development clashed with their over-protective and at the same time thwarting and limiting parents, and as a direct result developed a not inconsiderable degree of constant tension which could be exteriorized by either psychological or somatic factors into an actual attack of asthma. He stressed the importance of the basic tension, and warned that it might be manifested by fatigue, which is not due to exhaustion but rather to long-continued nervous tension. This assessment is, of course, in strict accord with the fundamental principles of psychosomatic medicine, which insist that the nervous tension which is responsible for any degree of somatic disease arises as the result of the activation of a basic conflict by some present life situation. The main factor, of course, is the basic conflict, which to all intents and purposes is at the subconscious level. The patient is no doubt aware of the difficult life situation, but is not conscious of the fact that this is merely the trigger mechanism which explodes his conflict. Appreciation of this fundamental principle is necessary before we can employ psychotherapy in the management of the allergic subject.

Rogerson's contention that the allergic personality is to some extent in-born is of profound importance. He is strengthened in his belief because it does appear as if these people are of a higher grade of intelligence than others, and so perhaps we are dealing with a special type of individual. I think it is germane to this theory that Sir Macfarlane Burnet, in his Stirling Lectures on allergy, has expressed the view that these people inherit a faulty gene which provides the mechanism whereby an antigen which is normally harmless is unrecognized as such by the allergic individual, and as a result a quite inappropriate reaction is provided in one of the shock tissues of the body, the characteristic allergic reaction being the result. I wonder whether Professor Burnet would agree that if one gene is faulty another may be, such as a gene that might be of importance in the psychological make-up of the individual. Every allergist recognizes that there are varying degrees of protein sensitivity, some slight, some severe. In much the same way there could well be varying degrees of inborn disturbance in the personality structure of the patient.

Be that as it may, we should recognize in the final assessment that there are people who have inherited certain defects in the field of allergy and in their psychological make-up, which in summation render them liable to one or other of the manifestations of allergy. The important thing to recognize, of course, is that either may be predominant in any one person. It may well be that the other is of minor importance, but in no case should it be neglected. Perhaps the less important factor may be the easiest to manage, and with adequate treatment the total sum may be reduced below the critical level at which allergic symptoms become manifest.

The rational approach to allergic disorders, then, includes not only a careful allergic history and protein sensitivity tests, but a searching psychosomatic history as well. I have found this not only invaluable in therapy, but essential in the assessing of prognosis. With this in mind I have endeavoured to classify the allergic disorders into four groups, according to the significance which I attach to the personality structures of the patients: (i) the allergic states with psychogenic factors at a minimum; (ii) psycho-allergic states in which emotional factors and allergic factors are each of significance; (iii) psychoneurosis with allergic disorders as a somatic manifestation; (iv) personality defect combined with a coincident allergic disease.

In the first group, in which emotional factors are to be regarded as of minimal significance, it follows that allergic factors are all-important. It is then incumbent on the physician diligently to pursue the search for the offending allergens. If they cannot be so determined from the history and sensitivity tests, then it is reasonable to conclude that either the investigation has not in fact been complete or the original diagnosis of an allergic disorder was wrong. Serious errors in diagnosis may in this way be avoided. When the specific allergen can be determined, then satisfactory results are generally obtained, either by elimination or by parenteral therapy designed to prevent the antibody-antigen reaction from taking place in one or other of the shock tissues.

The second group is possibly the largest and most interesting, in so far as the allergic and psychogenic factors are more or less of equal significance, and they provide a nice problem for the physician.

Obermayer, quoted by Dunbar, makes the following statement:

> The threshold of allergic response may be raised or lowered at a given time, by the state of emotional tension. A patient may react to an allergen at one time, but not at another.

Obermayer goes on to describe a child who developed asthma from the ingestion of fish at home, but the same fish failed to produce any reaction when the child was away from home.

Adequate therapy directed towards either the allergic or the emotional factor will probably greatly reduce the incidence of somatic manifestations, but I am sure that the best results follow treatment of both factors. These people are not to be regarded as psychoneurotic despite the tension under which they labour. Although it may not be apparent at first sight, I am of the opinion that this tension is fairly close to the surface and can be readily identified after one or two interviews.

Swanton some time ago suggested that allergic subjects all appeared to have a particular type of personality, variously described as nervous, irritable, excitable, aggressive, domineering, but also over-anxious, frightened and lacking in confidence. He was of the opinion that such aggressive traits were characteristic of the pre-asthmatic child, and that dependency and over-anxiety were the result of exogenous factors operating on these children. Such dependency then became a prominent feature of the full-blown asthmatic personality.

The more I see of this large group the more I am convinced that we are dealing with two classes of persons. On the one hand we have the somewhat aggressive person whose tension is almost entirely the result of exogenous factors, and on the other the rather dependent character whose tension is largely endogenous and appears to stem from an inborn error in personality structure. The resultant tension in both is more or less of the same pattern; but recognition of the fact that the psychopathology differs in each case is to my mind of vital importance.

Both types are frequently encountered in childhood, but the adult sufferer nearly always belongs to the latter group. I hold the view that the rather aggressive child, who is being frustrated by over-protective parents, tends to grow out of his asthma as he grows older and wiser, and what is probably more important, bigger and thereby more able to assert his independence. These are the children who do well if allowed to go to boarding school. On the other hand, the mother-dependent child, who tends to develop resentment when he feels that other members of the family are receiving preferential treatment, seems to carry this burden right through adolescence into adult life. At all events, in the fully developed adult personality it is easy to recognize the same dependent childish traits with evident resentment close to the surface. These people seem to think that life has not been fair to them. No doubt the life situation oftentimes is difficult, but it is rare to find them taking any positive steps to remedy it. As one observer has said, each attack of asthma represents a somewhat plaintive cry for help. From my case records I have taken two histories to illustrate my meaning.

The parents of a boy of seven years, an only child, consulted me regarding his aggressive behaviour. It appeared that during the preceding twelve months or so, he had taken to defying his parents openly. When mildly chastised, he would threaten to break windows, and had in fact hurled stones through no less than six. Further inquiries revealed that he had had severe asthma from the age of two years until twelve months previously. Throughout this period his mother stated that he had been a model child, docile and obedient. His asthma ceased about the time his aggressive behaviour commenced.

It is not common, at least in my experience, to encounter an adult asthmatic with these aggressive traits, no matter how repressed in childhood.

The second case is that of a small boy, of four years, who enjoyed a good deal of maternal attention until the advent of his baby sister. Thereafter he felt neglected. One night in the throes of an attack of asthma he confided to his mother: "Mummy, I like getting asthma, because then you cuddle me!"
(The emphasis was on "me".)

The prognosis for this child will remain uncertain whatever steps we take to counter his allergic state. I anticipate the same pattern of behaviour in adult life, resulting in a continuation of his symptoms. No doubt there are other conflicts which are responsible for the tension seen in this group, but in my experience hostility in frustrated aggressives and resentment towards life in their somewhat weaker brethren have been outstanding. I must admit I feel happier dealing with the first. However, as in all psychotherapy, it is important to give the patient or his parents insight into the origin of his symptoms. Sometimes it is enough; sometimes it is all we can do; but at least we can make some attempt to get the patients to express their resentment through healthier channels. Superficial psychotherapy such as this entails is well within the ambit of the average physician.

In this regard, although aware of the dangers of oversimplification, I like to quote from an article by Day published in 1946:

I have learned by experience in the Army Psychiatric Service that it is not always necessary to raise conflicts and forgotten traumata to the conscious level. In the vast majority of every-day cases, there is no more need to drag out—or drag in—the Ubiquitous Œdipal Situation than there is to invoke the Second Law of Thermodynamics when soldering a kettle.

The third group is a relatively small one, in which the major invalidity stems from the presence of an actual psychoneurosis. Here the allergic disorder may be regarded merely as a somatic manifestation. A careful history will establish the fact that we are dealing with a true psychoneurotic. These patients are disappointing from the physician's point of view, because the psychogenic factors are so predominant and the allergic factors so minimal that in the majority of cases no specific allergen can be detected. Even if we can discern an offending allergen, it is most unlikely that treatment along any allergic lines will have any benefit. Possibly the allergic disease is in the nature of a safety-valve protecting the patient from a more serious mental illness. At all events, such people must come under the care of the psychiatrist. As their anxiety remits, so will their allergic disorder diminish in frequency and intensity. There is no other treatment. Unfortunately, psychiatrists in the past have not been overhelpful in dealing with these patients because, taken by and large, they have tended to run for cover at the slightest whisper of organic disease. They certainly do not relish the prospect of being confronted one day with a patient in *status asthmaticus*. The fact remains that I can see no future for this group until such time as the psychiatrist realizes his responsibilities towards them.

And now consideration of the fourth and last group gives me an opportunity to emphasize the term "personality defect" as it occurs in clinical medicine. This description of a patient so frequently employed by psychiatrists has been altogether too much neglected by physicians, and yet I am convinced that it is in itself one of the most frequently encountered conditions in general medicine. Patients suffering with this handicap are falsely diagnosed as suffering from neurosis by a majority of doctors, even today.

I am satisfied that these people are not really seeking a cure for their complaints, but merely recognition of their invalidity, in order to bolster up their own inadequacy and afford a fit and proper excuse for their failures in life.

Should one of these people inherit a faulty gene which renders him liable to some allergic phenomenon, then I can assure you he is not going to part with it lightly. In this group the illness always appears to me to be motivated, and what is more, the motive is very close to the conscious level. There is no doubt in my mind that the patient has something to gain from his illness, and as a result is resistant to therapy from either an allergic or a psychiatric point of view. For my part, I take care before I include a patient in this group; but once I am satisfied that the classification is correct, then the only hope of success is to determine what the motive is and to try to deal with it.

There was a time when I used to exhaust all my therapeutic armamentarium and not a little of my patience in endeavouring to help these people, and as a result a feeling of resentment would be engendered when no progress was recorded. Since those days I have come to

regard them in much the same light as mental defectives. I can be sorry for them, but I do not intend to waste my time on treatment which I know will prove futile.

Some will object that when the allergic disease appears to be in the nature of conversion hysteria it should be included in the third group; but I find it occurring in this fashion so consistently amongst the people I have just described, and the results of treatment are so uniformly bad, that I have preferred to regard this type as a manifestation of personality defect.

This concludes my short review of the emotional factors which I think contribute to the so-called allergic diseases. Recognition of these factors of necessity involves a consideration of personality structure and the development of nervous tension in man. There are a number of physicians who maintain that such knowledge comes to us with experience and is to be regarded as the art of medicine. Such an attitude cannot be defended, and I am convinced that psychopathology can be taught *pari passu* with tissue pathology at the student level, and that stress should be laid on the fact that awareness of both is essential to the proper understanding and management of disease.

EMOTIONAL FACTORS IN ALLERGY.[1]

By H. J. Prior, M.B., B.S., D.P.M.,
Sydney.

Hippocrates is stated to have advised that the asthmatic person must guard against anger. In 1698 John Floyer published "A Treatise of the Asthma". Among the causes of the asthmatic fit he lists "passion" and writes:

> The Passion of Anger makes the Spirits restless and apt to produce the Fit and the Asthmatics observe in themselves great restlessness of Spirits the day preceding the Fit. Fear, Solicitude, and much study discomposes the Spirits and produces a restlessness in them which may occasion a Fit.

Since that time, and especially since about 1915 when anaphylactic phenomena were applied to the study of asthma, many authorities fail to mention emotional factors in this disease. Many others have paid lip service only; but more recently an increasing number of workers have returned to thought and investigation in the psychogenic field. I wish briefly to review some of the literature and to gain some orientation in this problem of the rather complex interplay of psychogenic elements in allergic reactions before discussing the psychopathology and indicating some points in management.

In the 1930's a team of allergists working in Columbus, Ohio (Mitchell *et alii*, 1947), regretfully realized that among their patients there were many whose symptoms they could neither explain nor understand, a group whose difficulties were not being solved by the search for new allergens or the presentation of new drugs, and in whom therapeutic procedures yielded no consistent or satisfactory results. A research programme was instituted and it was found that early in the history-taking it could be confidently predicted that the patient would fall into one of two groups: (i) positive reactors to skin tests who gave a rather concise and typical allergic history and responded satisfactorily to the usual therapeutic procedures of the allergist, or (ii) non-reactors to testing who gave a more detailed history incriminating all manner of dusts, foods, odours and fumes, who volunteered many apparently unrelated symptoms, and in whom therapy had in the past been disappointing.

Of the whole group, 22% were such "non-reactors" and they were studied in more detail. It then became apparent that the allergic symptom was only one facet of a larger psychosomatic problem. Approached from this broader angle, the picture was clearer. Many patients were helped who would previously have "drifted" and been classified as failures in allergic management.

Many of these psychologically maladjusted patients made statements of confusion, conflict, hostility, fear, family or office troubles, guilt feelings, and social inadequacies, but "the most common sources of conflict could be traced to difficulties in personal relationships within the home circle which had usually been conditioned by childhood experiences".

Although the above rather clean-cut grouping was made, these workers, like so many other authorities, are careful to point out that in the individual patient physical and psychological factors are often closely interwoven and careful evaluation is necessary in both diagnosis and treatment.

In 1939 McDermott and Cobb reported the results of their psychiatric survey of 50 cases of asthma. Their patients were an unselected group from the anaphylactic clinic at Massachusetts General Hospital. These workers were particularly interested in the presence and role of emotional factors in asthma.

The average age of the patients was thirty-seven years. In 26% of cases no relevant psychological factors were discovered. In 14% these factors were doubtful, but in the remaining 60% emotional reactions were clearly implicated, either as precipitating or as aggravating causes of the asthmatic attack. The type of emotional upset will be considered at greater length, but in general the disturbance was found in marital, domestic, occupational, economic, sex, or family stress. Some other findings may be summarized:

1. Of the total, 40% considered that emotional experiences had precipitated the first attack, whilst 52% claimed that subsequent attacks were often caused by emotion.

2. Of the whole group, 68% gave positive results to skin tests but there was no significant difference between the "emotional" and "non-emotional" group.

3. The average age of onset was about the same for both groups.

4. Of the whole group, 60% were adjudged "neurotic", and of these, two-thirds of the total number were in the "emotional" group.

5. In the "non-emotional" group 54% claimed considerable benefit from somatic therapy as compared to 20% in the "emotional" group.

6. Similarly, 50% of the "non-neurotic" were improved by physical means as compared to only 20% in the "neurotic" group.

These two last-mentioned findings were held to be of added interest because certain cynics have maintained that the usual somatic therapy for asthma is effective chiefly as a result of the element of suggestion! If such suggestion played a major part one would, of course, expect much better results in the suggestible "neurotic" and "emotional" patients.

In 1944 Fishman investigated the ætiological factors in 100 consecutive patients evacuated from battle areas to the United States of America. Some of his findings were:

1. Of the 100 patients, 56% developed asthma for the first time overseas. The remainder had had mild attacks in civilian life but had never before been completely incapacitated.

2. Thirty-one of the 56 who first developed symptoms overseas had a positive family history of allergy, predominantly asthmatic, and therefore a behaviour pattern was available to them which could be utilized in time of stress.

3. In this group of 56 it was considered that in 15 instances the symptoms could be unequivocally ascribed to allergy. In 14 there was evidence that ætiological factors were entirely psychogenic, and in the remaining 27 cases the relative importance of allergic, emotional and infective elements could not be adequately assessed.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on May 31, 1951.

4. Few patients would admit fear as an aggravating or precipitating cause, but many thought that worry facilitated an attack, and it is interesting that the majority of attacks occurred at night just after they retired.

5. Seventy-eight of the whole group were asymptomatic on arrival in the United States of America and required no further treatment prior to discharge from the services.

Fishman maintains that some illnesses, previously ascribed to intrinsic allergy, are in reality largely caused by psychogenic factors. In this particular group of patients exposed to the psychological traumata of war he considers that emotional factors are of paramount importance. He concludes:

> Many of the cases included in this report fall into the group of constitutionally predisposed individuals who have had previous chest involvements and superimposed fear of lung diseases. Their attacks may then represent imitations of similar attacks which were previously observed in their families, and closely mimic asthmatic breathlessness. It is obvious that for this type of patient psychotherapy would be more effective than any type of somatic therapy.

The work of Rogerson at Guy's Hospital is well known (Rogerson, 1937). His chief interest has been in children suffering from asthma or eczema-prurigo, or both together. There was a curious similarity in the histories and personalities of his patients. "Nervousness" was volunteered as a leading complaint in 23 of a group of 30 patients thoroughly investigated. Restless, irritable behaviour was found in 22; insecurity, over-anxiety and fearfulness in 21. Nineteen showed aggressive, irritable and dominating behaviour in frustrating circumstances. Such findings did not appear to any unusual degree in the control group.

In 18 cases one or both parents were over-anxious and over-protective to a pathological degree. There was often evidence that this attitude had been present prior to the advent of allergic reactions in the children.

In 14 patients 43 actual attacks were fully investigated. It was considered that the attack was primarily due to mental conflict in 33 of these, but that it represented an escape mechanism or desire for sympathy in only three cases and was reflexly conditioned in two. Rogerson maintains that on many occasions the relationship of emotion to the attack was clearly demonstrated. Attacks tended to increase when there was tension between the parents. A patient who remained well for up to two years in the convalescent centre often responded with an attack when the parents called to take him home.

Such findings, gleaned from but a small proportion of the relevant literature, indicate that emotional factors are often significant in allergy and that they can render somatic therapy ineffective.

Ætiological Factors in Allergy.

At this point I feel it will be an advantage to refresh our memories of the broad ætiological factors in allergy.

Miller and Baruch (1948) point out that clinical allergy must be differentiated from immunological allergy. From the latter viewpoint allergy is constitutional and can be established by demonstrating the offending antibody. (Incidentally, it is not claimed that psychogenic elements produce immunological allergy, although the clinical manifestations may be identical.) However, eczema or urticaria may also be produced by non-allergic factors such as infective, chemical, radiant or mechanical trauma, possibly by endocrine anomalies and, it would appear, by emotional conflicts.

Therefore the individual patient may or may not be immunologically allergic, and in any case one of the above factors may precipitate an attack at one time and another agent operate on another occasion. More often it seems likely that two or more causes summate or interact to produce the clinical episode. Trousseau is reported to have observed in himself that when calm and unruffled he could inhale oats dust with equanimity. But if in the vicinity of the stables he also became angry with his coachman he reacted with an attack of asthma. Rogerson reports the same phenomenon in his patients. A child who responds to the ingestion of fish at home with violent allergy can eat the same type of fish without upset whilst in hospital. In such instances we are forced to think in terms of multiple, and sometimes complex, interacting factors and to abandon "the sole cause" of disease so beloved by medical tradition.

The Emotional Factors.

What then are these emotional factors of significance in allergy and how do they operate?

Precipitating, Aggravating or Alleviating Factors.

Almost every stress and strain to which the human mind is heir has been implicated as a precipitating cause of allergic reactions—upsets in family, marital and domestic life, illnesses, shocks, deaths, jealousy, quarrels, infidelity, marital separation, sex difficulties, worry over the children, difficulties with drunken or maladjusted parents, housing difficulties, in-law problems, pregnancy of the mother, the advent of other children, the stress of physical, mental or social inadequacies, the upheavals of war, financial and economic strain, occupational maladjustment and so on, right down to the excitement of a football match, war pictures, getting married, and even "anxiety dreams".

Emotional tension in the sex sphere receives "honourable mention" in most of the literature. Stokes and Beerman (1940) quote a case of Dunbar's. This patient acquired a sadistic partner who delighted in raising large welts upon her skin with the aid of a belt. The lady felt she should dismiss her lover for such behaviour but ardently desired to retain his attentions. She made a nice compromise and by "raising her own welts" at appropriate times succeeded in both holding her partner and avoiding the beatings.

The emotion of anger frequently precipitates, aggravates or alleviates the asthmatic or urticarial outburst. McDermott and Cobb (1939) write of a middle-aged man who suffered for years with severe asthma. When he was admitted to hospital all his bottles, pills, powders, atomizers and incense burners were confiscated. The staff was forbidden to give any medication. He quickly developed a terrific reaction and when eventually confronted by his firm and adamant physician flew into a violent rage; his wheezing stopped forthwith. A woman asthmatic always developed asthma after marital quarrels but found that if she became "very angry" or "really enraged" the attack subsided almost at once. Another young asthmatic with considerable conflict over auto-erotic practices discovered that if he actually indulged his habit whilst in the throes of an asthmatic attack the paroxysm ceased.

The relationship of the emotional disturbance and the autonomic reaction to the allergic attack in these cases appears clear. Such patients carry their own "hypodermic of adrenaline" with them, but I feel that the therapeutic implications are rather limited.

In general it appears certain that the development of emotional tension, from whatever cause, very often does favour the allergic explosions, whether the actual match that sets it off is of physical or psychological origin.

Psychopathology.

The allergic reaction has been variously interpreted as an expression of hostility, aggressiveness, domination or self-punishment.

Undoubtedly a constitutional weakness or allergic predisposition is present in many cases, and the skin, nose or respiratory system may be utilized in the expression of emotional conflict in much the same way as another person will produce "hysterical paralyses" in a limb which has been the site of previous weakness or disease. Moreover, earlier respiratory disease does appear to condition the soma for later attacks of asthma in some cases, and even a preexisting fear of lung disease may play this role. Strauss (1935) indeed goes further. Many psychoanalysts claim that the mind contains a partly or completely uncon-

scious picture of our internal anatomy and physiological function. This conception may be grossly inaccurate or distorted but still play a part in the production of psychogenic symptoms. By way of illustration, Strauss recalls a joke from *Punch* in which a mother finds her small son standing in a corner puffing and blowing at a great rate. She asks what he is doing and receives the reply: "I'm killing Chinamen." Asked to explain this extraordinary statement he answers: "Nanna told me that every time one breathes a Chinaman dies." Strauss holds that certain asthmatic attacks may represent the working out of some such confused fantasy concerned with respiratory function.

There is no doubt that the behaviour pattern and emotional reactions of parents and others intimately associated with the child may modify and colour subsequent mental processes and behaviour. Some allergic reactions may well depend on such suggestion, or on imitation of such attacks previously witnessed. "Conditioning" may also be a factor, and the "secondary gain", such as the gaining of sympathy and care, occupation of the centre of the family stage, the evasion or escape of responsibilities *et cetera*, may all play their part.

The spotlight, when turned more fully upon the psychoanalysts, reveals, as usual, food for somewhat deeper thought. They have frequently found that as asthma becomes less during the analysis it is replaced by fits of crying to which there had been no previous addiction. At other times the asthmatic attack ceases if the patient begins to weep. In such cases the asthmatic paroxysm is often regarded as equivalent to a cry of anxiety, or as the expression of hostility and aggression with repression or inhibition of the cry of rage. Saul (1941) feels that the site of expression in asthma is determined by a sudden threat to the attachment to the mother with repression of the resultant tendency to cry out.

Other analysts agree that the specific situation in which an attack often results is the threat of estrangement from the mother—in fact, in fantasy or in dreams. As one would expect, this occurs frequently in the sexual field, as for example when the child developing sex curiosity is rudely repulsed by the "mid-Victorian parent"—with the resultant threat of deprivation of mother love. It seems significant that in the analytical situation attacks are often found to occur preceding separation from the physician, who presumably has become a parent figure or substitute.

The findings and hypotheses of Saul are particularly impressive. He feels that the emotional factor in allergic manifestation is constant. In general he considers that a state of repressed but intense frustrated longing, basically for the mother, is fundamental. The resultant emotional reaction leads to physiological changes which may imitate the symptom of allergy, or may sensitize the tissues to allergens so that they respond to otherwise subclinical doses of the physical agent. (It also seems probable that if a particular tissue is irritated by allergens it will be this site which is likely to react to emotional stimuli.)

In view of Saul's emphasis on the mother relationship, it is significant that Miller and Baruch found that maternal rejection occurred in 62 of the 63 allergic children investigated by them. It is also of interest that these workers, like Rogerson, found that maternal over-protection was often evident, actually proven in the case of 36 of the 63 mothers, and that sex maladjustment was a frequent finding in the parents. I feel that I should "pass on" the statement of one of these mothers who was rapidly gaining "insight" into the problem. Whilst in conversation with her physician she suddenly burst out: "It's one thing if my boy was sensitive to eggs; I would do something about that. But if it's my sex life that's affecting him, he can just go on coughing the rest of his life."

The findings of anxiety, insecurity, hostility and aggressiveness *et cetera* in so many allergic children may well be due to the influence of secondary mechanisms based on the more fundamental psychopathology indicated above. The rather characteristic "asthma-prurigo personality" found in children, and the marked tendency to an obsessional type of personality in adults (Brown and Goiten, 1943) also becomes intelligible on some such basis. Thus, some children may seek to avoid rejection by "over obediency", others attempt to "compensate" by gaining sympathy and attention; others again react with hostility, with aggressiveness or with similar "protests" and "defences" against the real or imagined threat to the dependent attachment to the mother, or mother substitute.

The question of the hen and the egg, as to which came first, must also receive consideration. Some authorities maintain that the emotional or personality changes result from the affliction and are not in themselves causal. I do not doubt that this factor is important in many cases. A severe paroxysm of asthma, perhaps in the eerie hours before dawn, with a small child in distress as it clutches the bed and fights for breath, is a terrifying experience for all concerned. One must expect psychogenic complications in a proportion of such cases—the growth of "over-protection" in parents, the unhealthy reflections of parental fear, and the development of mechanisms furnishing "secondary gains" in the child. The irritation, discomfort, economic loss and social inferiority associated with chronic skin reactions must also have a significant effect on the psyche in many, if not all, sufferers. The final evaluation of the various findings may not be easy or indeed always possible, I feel, in the individual patient.

Points in Management.

1. Simple reassurance and explanation, especially in the case of initial attacks of asthma, and including children, their parents and adult patients, would seem sound preventive medicine. Such reassurance *plus* the friendly support and security of the family physician must be an invaluable link in the chain of therapy and prevention.

2. When the question of a fuller psychosomatic history and more intensive psychotherapy arises, the "time factor" inevitably raises its ugly head. As to how far the general practitioner can proceed must depend upon his time, enthusiasm, patience and knowledge. A goodly proportion of patients, I feel, must go on to the clinic or consultant for adequate investigation and therapy.

3. In the allergy clinic a full psychiatric team of psychiatrist, psychologist and social worker appears essential. Therapy with the parents will often be as important as with the allergic child, or even more important. As some practical psychologist once said: "Got t' judge the owner as well as the hoss, and if there's anything the matter with his conscience it'll come out in the hoss somewhere." In general the over-protective parent must be persuaded to give the child his chance to develop normally, a chance to develop independence even though it may mean falls from trees and fences, shattered shins and patched pants. The child in his turn will need reassurance, support, encouragement and often "reeducation" and a chance to express his difficulties through other channels—perhaps through the medium of play therapy. In some cases the question of environmental manipulation will also arise at times. The adult patient is perhaps more easily "judged on his merits". If the history of seasonal, environmental, or infective agents is clear and somatic therapy effective, there is of course no necessity to question the psyche. But if the longer psychosomatic approach is indicated the attempt to relieve emotional tension, from whatever source and by whatever means, should pay dividends. In many patients superficial assessment and simple psychotherapy only may be desirable, but it seems probable that nothing short of full psychoanalysis will be effective in a minority.

4. As a final point in management the importance of reasonably early and adequate therapy is stressed. Unrecognized or neglected unhealthy attitudes and abnormal patterns of response become habitual and closely interwoven in the personality. The secondary gains, conditioned fears, and other reactions will in themselves then present a major therapeutic problem.

Conclusions.

1. The relationship of emotional factors to allergic sensitivity has not yet received a completely final answer.

2. It seems certain that emotional factors can precipitate, prolong, modify or prevent the allergic attack. (In certain patients no attack will occur, even in the presence of allergens, if emotional factors are removed or controlled.)

3. The complete psychopathology of the individual case may cover a wide field and present an intricate superstructure of secondary reactions and manifestations as well as more basic psychopathology. But in any case psychiatric assessment would often appear desirable for complete understanding of the patient and his situation, and psychotherapy necessary if the process is to be arrested and possible complications, both physical and psychic, prevented.

4. In just what proportion of the total allergic population these emotional factors are sufficiently important to warrant more detailed investigation is not very clear. My impression is that the figure would be at least 20% and quite possibly nearer 40% or 50%.

In conclusion I should like to quote the words of Macfie Campbell speaking before the College of Physicians in Philadelphia in 1938:

> Happy the specialist who has a well-defined vocabulary at his disposal, who works in a field where the terms are technical and explicit, who can give an ocular demonstration of the object to which he refers, who can isolate the dynamic system of which he talks! Unhappy the psychiatrist whose language is a blend of ordinary speech with its lack of precision, and of technical terms whose apparent precision masks misleading assumption and great divergence of opinion!

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THE OSMOTIC THEORY OF ECLAMPSIA AND THE MECHANISM OF WATER RETENTION.

By J. C. EDWARDS, B.M., B.Ch., M.A.,

Department of Public Health, Perth, Western Australia.

THE OSMOTIC THEORY OF PREECLAMPSIA.

IN a previous paper on preeclampsia (Edwards, 1950) I proposed what might well be called the "osmotic theory of toxæmia of pregnancy". I showed that on the basis of figures (Cummings, 1934) relating to the average weights of pregnant women, the full-term weight of the patient was increased by an average of ten pounds more than could be accounted for by the weight of the fœtus, placenta, *liquor amnii*, enlarged uterus *et cetera*. As this excess of weight disappears rapidly after delivery, it appears to be fluid which is no longer retained after the emptying of the uterus. It was proposed that this physiological change was initiated by the power of the mineralo-regulatory hormones (desoxycorticosterone and progesterone) to concentrate electrolyte intracellularly, which raised the osmotic pressure across the cell membrane. This pressure was then partially neutralized by an increase in the water and electrolyte content of the extracellular fluid and blood plasma.

Such a conception receives support from other authorities. Dieckmann *et alii* (1949) show that the ability to excrete water and electrolyte is reduced in the pregnant patient as compared with the non-pregnant patient. In the preeclamptic patient this aberration from the normal is greatly exaggerated. Parviainen *et alii* (1950) experimented with pregnant rabbits, giving them five milligrammes of "Percorten" daily. The authors think that in addition to the retention of extracellular sodium, the sodium is also retained intracellularly, as the sodium retention is relatively greater than could be accounted for by the increase in extracellular fluid. It has been shown that a single injection of desoxycortone acetate causes sodium to penetrate the cells of a healthy, non-gravid individual. Also the authors state that the pathogenetic mechanism of desoxycortone intoxication is similar to that of toxæmia of late pregnancy.

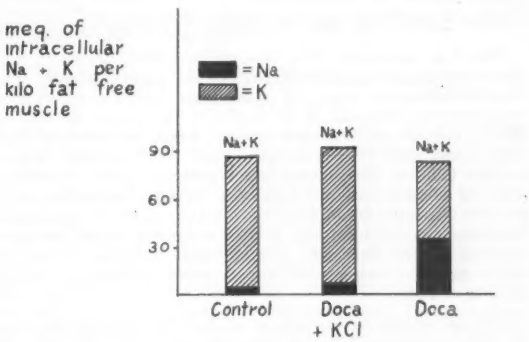

FIGURE I.

The intracellular replacement of potassium by sodium in the muscles of normal dogs under the influence of desoxycorticosterone (DOCA). The effect is inhibited by the administration of potassium chloride. (After Loeb.)

Earlier work by Loeb *et alii* (1939) is similar. Loeb injected DOCA into normal dogs and found that the intracellular sodium-potassium ratio was much increased. Thus the cell released the potassium ion and absorbed the sodium ion. If potassium chloride was given simultaneously, the alteration in the sodium-potassium ratio was inhibited, but the total intracellular electrolyte content was increased. In my previous paper I suggested that if one assumed that the intracellular concentration of the potassium ion was increased, as in column II of Loeb's diagram, then the water retention of pregnancy could be explained by the power of osmosis and the Gibbs-Donnan laws relating to membrane equilibrium. This increase in the osmotic power of the cell depends upon the greater energy of the sodium ion over the potassium ion in its ability to penetrate the cell membrane. Kelsall (1951) finds that in preeclamptic patients there are found in the extracellular fluid a relative decrease in the sodium ion and increase in the chloride ion, owing to movement of sodium into the cell which takes place at the expense of the alkali reserve; this consists of sodium bicarbonate in the blood. These changes do, in fact, suggest an increase in the osmotic pressure of both the intracellular and extracellular solutions, and hence produce that state of affairs which I attributed to a simple increase of intracellular ions. These changes take place under the influence of cortin and progesterone. The increase in the activity of these substances is dependent upon the presence and secretory activity of the placenta. The placenta is known to secrete three hormones, œstrone, œstriol and chorionic gonadotrophin; the last-mentioned is assigned the role of regulator of the steroid hormones,

which control osmotic power of the cells. Once this hormone is removed or neutralized, the osmotic basis of preeclampsia disappears. This probably accounts for the success which attended the Smiths (1949) in their use of diethylstilbœstrol as a prophylactic against toxæmia, as it is known that the œstrogens inhibit the activity of the pituitary hormones.

I then argued that the osmotic effect of the mineralo-regulatory hormones would not be effective in initiating water retention unless the kidney reacted in such a way as to retain the extra fluid absorbed into the body. There are exceptions to this, in that Dieckmann has had three patients with *diabetes insipidus* who have shown œdema during pregnancy. Nevertheless, there is evidence that the principle is there in general. Verney (1947) has shown that the antidiuretic hormone of the posterior lobe of the pituitary is stimulated by an increase in the osmotic power of the extracellular fluid due to the ionic electrolytes, mostly sodium chloride, of the extracellular fluid. This means that the osmotic effect produced by the steroid hormones will react indirectly upon the antidiuretic hormone of the posterior lobe of the pituitary, and hence the retention of fluid and electrolyte will be accentuated.

The Action of the Posterior Pituitary Principle.

There is evidence that the reabsorption of water takes place mainly in the second part of the loop of Henle, where the epithelium is thin. It is assumed that the effect of the antidiuretic hormone is to increase the power of the cells of the tubules to reabsorb water; what is the meaning of this statement? Presumably, that the hormone initiates in the tubular cells some vital process which causes the cells to absorb water. However, by what physical or biophysical means could this be brought about? Osmosis or filtration by hydrostatic pressure is the usual means of passing water through a membrane. There is, in fact, much mystery concerning the process of tubular reabsorption of water.

Let us return to the action of the hormone or hormones of the posterior lobe of the pituitary in general. The principle which affects the melanophore cells of reptiles is derived from the *pars intermedia* and not from the posterior lobe proper, and therefore need not be considered further. There are two preparations of the hormone—oxytocin and vasopressin. The former is standardized for its oxytocic activity and the latter for its effect upon the blood pressure. However, both fractions do, in fact, show the double activity to some extent. For the purposes of this study it is unnecessary to distinguish between the two fractions. Hence the term "posterior pituitary principle" will be used to cover the physiological activity of the posterior pituitary body as an endocrine organ.

The effects of the posterior pituitary principle may be briefly summarized, the action of the antidiuretic hormone being for the moment omitted.

1. The blood pressure is raised, and this is accompanied by pallor of the skin. This mechanism arises from constriction of the arterioles and capillaries. This is due to a contraction of the smooth muscle of the arteriolar wall and to a direct action upon the capillaries, which are therefore contractile under the influence of the posterior pituitary principle.

2. Plain muscle is stimulated by the posterior pituitary principle. The organs affected by this action are those containing smooth muscle within their walls, such as the uterus, the intestine, the gall-bladder, the ureters and urinary bladder and the mammary alveolæ and ducts (galactagogue action).

From what has been discussed so far, it is possible to make a generalization as follows: the action of the posterior pituitary principle is due to its ability to cause the contraction of smooth muscle. Later the possibility of including the action of the antidiuretic hormone within this generalization will be discussed.

The Problem of Tubular Reabsorption of Water.

Smith and his associates (1941) found by means of the inulin clearance test that the quantity of filtrate formed in the human kidney was 125 cubic centimetres per minute. Normally about 99% of this is reabsorbed. Hence, the kidney can reabsorb approximately 125 cubic centimetres of fluid per minute. At first sight this seems a remarkable feat upon the part of the cells of the renal tubules.

In the kidney of the frog the glomeruli are not continuously patent (Richards and Schmidt, 1922), and under chemical and nervous stimuli the number of patent

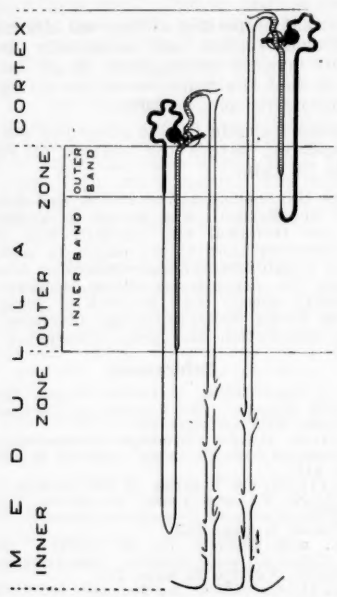

Figure II.

Diagrammatic representation of cortical and juxta-medullary nephrons. Malpighian corpuscle and proximal convoluted tubule in black; distal convoluted tubule shaded. Circle represents the juxta-glomerular apparatus, in the structure of which the afferent artery passes under the distal convoluted tubule. Note that sphincteric constriction at this point will convert the nephron into a closed sac. Hence, any further filtrate entering Bowman's capsule will cause filtrate to be expelled through thin segment of Henle's loop. (After Trueta.)

glomeruli varies, hence altering the amount of filtrate which is created. In man there is evidence that the glomeruli are more continuously patent (White, 1939). However, the frog has no thin segment of Henle's loop and hence cannot reabsorb water under the influence of the antidiuretic hormone of the pituitary in exactly the same way as the human kidney. Antidiuresis in frogs is likely to be due to the active contraction of their glomeruli. Frogs increase their weight when injected with the posterior pituitary principle. Therefore, the posterior pituitary principle has an antidiuretic effect also in frogs.

The arguments against the tubular reabsorption of water by the kidney are as follows. (i) Difficulty exists in explaining the vital process in biophysical terms. (ii) The disease of *diabetes insipidus* demonstrates that osmosis is not the only factor involved. (iii) The cells of the thin segment of Henle's loop are not the robust type of cell which suggests ability to carry out a vigorous "vital process"—in fact, they are the very reverse, as they are more suggestive of a semi-permeable membrane capable of

filtration. (iv) Antidiuresis takes place in the frog under the action of the posterior pituitary principle, although the frog has no thin segment of Henle's loop. In the frog, at least, the posterior pituitary principle must act upon cells of the vascular system, not of the tubular system—that is, the action of the hormone is proximal to Bowman's capsule and not distal to it. This is consistent with the statement that the posterior pituitary principle acts primarily upon smooth muscle.

The Goldblatt Mechanism as a Physiological Compensatory Process.

It has been shown by Goldblatt and others (1934) that the ischæmic kidney (that is, a kidney supplied by a clamped renal artery) produces the activating agent of a vasopressor substance. This mechanism is as follows. The ischæmic kidney produces a substance, renin, which activates a pseudo-globulin hypertensinogen. It is known that an enzyme hypertensinase is capable of inactivating hypertensin. Thus:

Renin + hypertensinogen → hypertensin (activation)
Hypertensin + hypertensinase → (inactivation).

Under the action of hypertensin the blood pressure is permanently raised and the efferent arteriole of the glomerulus is constricted, increased filtration pressure being caused. It is believed that it is the ischæmic renal cortex which produces renin, but it is not known what part of the cortex produces this substance. Goormatigh has suggested the juxta-glomerular apparatus. An alternative possibility is the proximal convoluted tubule.

Let us now assume, what is difficult to prove, that Goldblatt demonstrated in his means of producing hypertension a physiological compensatory mechanism. We find that hypertension is produced in those conditions in which there is an inadequate flow of blood through the glomerular system as a whole. In chronic nephritis, in which the number of glomeruli is reduced by the disease, the compensatory mechanism ensures that the filtration through the remaining active glomeruli is increased. Furthermore, if we assume that renin (not hypertensin) normally escapes from the body by way of the glomerular filtrate, we can see that we have an automatic means of increasing glomerular filtration as soon as it falls below the minimum required to eliminate renin. Hypertension arising from hypertensin is essentially a means of eliminating fluid from the body, and is therefore diametrically opposed in this respect to the increase in blood pressure due to the posterior pituitary principle, in which fluid is retained to a greater extent through the action of the antidiuretic hormone. It has yet to be shown or disproved that the contents of an ischæmic pregnant uterus produce a vasopressor substance. If they do, we should on teleological grounds expect its action to resemble that of the posterior pituitary principle rather than that of hypertensin.

Trueta's Studies of the Renal Circulation.

Trueta (Trueta *et alii*, 1948) has shown that under normal circumstances the circulation of the kidney passes through the glomeruli of the cortex of the kidney. Under certain abnormal conditions nearly the whole circulation is diverted into the juxta-medullary glomeruli and to the intertubular vessels of the medulla, and the blood emerges a bright red in the renal vein. Under such circumstances the kidney blanches, much as the cheek does under the same conditions. The conditions necessary for such a deviation of the renal circulation are the application of a tourniquet to a limb, the injection of adrenaline or posterior pituitary principle, the intravenous injection of staphylococcal toxin or nervous stimuli. These experiments show that the kidney is under the influence of both nervous and hormonal control. Fulton (1950) shows that the secretion of urine is partly under the control from area 13 of the cerebral cortex. Cort (1949) also finds that Trueta's renal shunt can be activated by afferent nerve stimulation, and also by stimulation of the vasomotor centre of the medulla, the posterior hypothalamic nuclei and area 13 of the cerebral cortex.

Comment.

Hence, it can be said that anuria may be caused mechanically through nervous control of the renal vascular system, and that the posterior pituitary principle may also be the activator of this mechanism.

However, in spite of all this circumstantial evidence the real solution to the problem of tubular reabsorption of water is provided only by a careful and accurate study of the micro-anatomy of the nephron and glomerulus. Such a study has been provided for us by Zimmermann (1933).

The Anatomy of the Nephron.

The nephron consists of the following: (i) the renal corpuscle, which is constituted of the glomerulus and Bowman's capsule; (ii) the proximal convoluted tubule; (iii) the loop of Henle; (iv) the distal convoluted tubule. The points of note are that Henle's loop is in part lined by clear flattened cells, and that the length of this part of the loop is greatly increased in the juxta-medullary glomeruli. Finally, it must be noted that the distal convoluted tubule comes into contact with the afferent artery of the glomerulus within the structure of the juxta-glomerular apparatus. What is the significance of these special anatomical relationships, and what are the functions of the juxta-glomerular apparatus?

The Histology of the Renal Corpuscle and Its Adjacent Structures.

Let us consider first the glomerular cells. By the Golgi-Kopsch method the endothelial cells of the glomerular capillary of the cat were shown to contain a condensation of the cytoplasm forming a network throughout the cell and continuous with the nucleus. The supporting cells of the glomerular capillaries are of various types, the cubical, the "band type" (Figure IIIB), the "net type" (Figure IIIC), and the fir-branch type (Figure ID) of cells. The three last-mentioned types of cell are all characterized by their individual cytoplasmic condensations. Besides these cells, strands of connective tissue cells which grip the capillaries, and pericytes which pierce the capillary basement membrane with button-like processes or "little intracapillary protuberances", can be demonstrated (Figure IIIE).

We know that all capillaries are capable of contraction under the appropriate nervous or chemical stimulus. We know also that the hydrostatic pressure entering the glomerulus is at times very considerable. For these reasons it is obvious that the glomerular structures require considerable tensile strength. Hence, we may expect that the functions of these various cytoplasmic condensations will be contractile and tensile.

The next structure to be considered is the juxta-glomerular apparatus. This structure consists of the afferent artery, the *macula densa* of the distal convoluted tubule and the encircling muscular fibres. It is well shown in Figure IV, but unfortunately in this illustration the pole cushion is unusually poorly developed.

In the afferent artery of some mammals the endothelial cells can be shown to be tearlike in shape, the blunt swelling of the "tear" being nearest to the glomerulus. Similar cells in the efferent artery have been shown only by Zimmermann to be present in the bear. On the outside of the vascular pole at this point there may be found in all mammals short ellipsoid cells in the wall of the afferent artery directly following on the smooth muscle fibres. These ellipsoid cells form the "pole-cushion", and they are embedded in a scaffolding of muscle fibres which embraces the arteries, the distal convoluted tubule and the *macula densa*, and the vascular pole of the glomerulus. The presence of transitional forms between the cushion cells and smooth muscle fibres points to a genetic relationship. These are therefore myo-epithelioid cells. The *macula densa* is that part of the distal convoluted tubules lying within the juxta-glomerular apparatus, whose cells assume a columnar shape and have densely packed nuclei, the whole structure having a plaque-like appearance. The

endothelial "tear" cells protrude into the lumen of the afferent arteriole. This is well shown in Figure V, and it is obvious that the passage of blood cells, and hence of whole blood, would be impossible under the condition of arteriolar contraction shown in this illustration.

For the reasons given above, we may now propose the hypothesis that nervous stimuli and the posterior pituitary principle act upon and control the tone of the muscle-fibre scaffolding of the juxta-glomerular apparatus, and that the enclosed part of the distal convoluted tubule acts as a sphincter occluding the termination of the renal tubule. In the fully relaxed state of the juxta-glomerular apparatus, the blood from the cortex will pass through the glomeruli at high speed and at high pressure. The nephron will therefore offer no resistance to the passage of the filtrate. These conditions exist during diuresis in normal subjects, and permanently in the patient with *diabetes insipidus*. Under normal conditions, therefore, a definite tone will be exerted in the muscle fibres of the apparatus, and hence both the pressure and the flow of the blood in the glomerular capillaries are reduced. Thus less filtrate is formed, and also the exodus of the filtrate from the tubules is obstructed by a weak pressure at the *macula densa*, and the filtrate will be held for some time within the tubules. This gives an opportunity for the cells of the tubules to absorb certain metabolites, to excrete unwanted substances and to allow water to pass back into the blood-stream through the thin portion of Henle's loop under the influence of osmotic pressure from the plasma proteins and a hydrostatic pressure within the tubules themselves, causing some backward filtration. Extreme contraction of the apparatus would completely cut off the blood supply of the glomerulus. On accepting this hypothesis we may reject the theory that the tubules are capable of actively "reabsorbing" water.

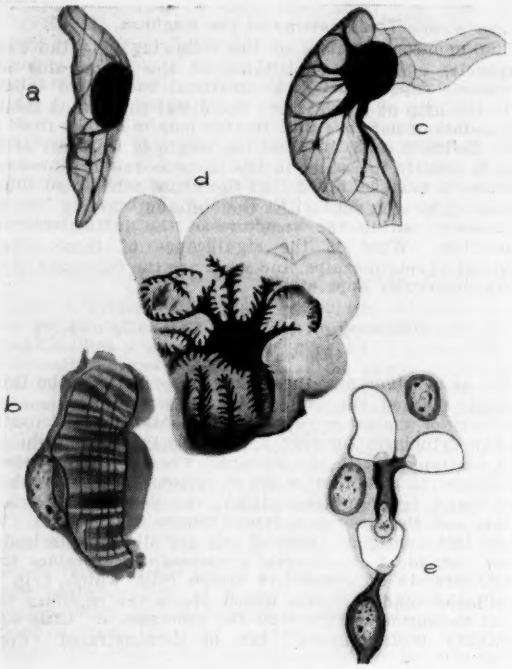

FIGURE III.

After Zimmermann. (*a*) Cat: Golgi-Kopsch chrome-silver method. An endothelial cell of a glomerular capillary, showing a network of slender cytoplasmic condensations spreading from the protuberance containing the nucleus into a veil of thin cytoplasm. The right cell shows three "basal frills". (× 1066.) (*b*) Squirrel kidney: fixed with Tellyesniczky formol injection and stained with von Mollendorf's iron hæmatoxylin. Glomerular capillary with typical cross-banding of the supporting cells due to slender parallel subendothelial threads. (*c*) Cat kidney: Golgi-Kopsch chrome-silver method. A supporting cell of the "net" type from a glomerulus. The processes originating from the nuclear substance and branching frequently are condensations of a thin continuous veil of cytoplasm. (× 1066.) (*d*) Hedgehog kidney: Golgi-Kopsch chrome-silver method. Portion of a glomerular lobule close to the peripheral end of the corpuscle. Supporting cell of "fir branch" type. (× 1066.) (*e*) Rat kidney, fixed by Tellyesniczky *formol injections*; Azan stain. Showing the peculiar relationship of fibrocytes to the glomerular capillaries. Note formation of small intracapillary protuberances, which are situated sub-epithelially, as shown.

FIGURE IV.

After Zimmermann. Ox kidney: Azan stain. This shows the afferent glomerular arteriole traversing the "pole cushion". There is a transition of smooth muscle into "pole cushion" cells. Note that when the muscle scaffolding of the apparatus contracts, as shown, the "tear" cells are pressed together within the lumen of the arteriole, which is thus completely blocked. (Transverse section.)

THE ASSOCIATION OF THE HYPOTHESIS WITH THE DISORDERS OF PREGNANCY.

Acute Cortical Necrosis.

Acute cortical necrosis arises under severe stimulus of the type induced by Trueta. An excellent example of the type is seen in accidental hæmorrhage, and there are two factors involved: (i) There must be a diversion of fluid from the vascular system, as in hæmorrhage or shock, and hence a reduction in systemic blood pressure. (ii) There must be prolonged nervous or chemical stimulation of the juxta-glomerular apparatus and complete deviation of the blood supply of the glomerulus.

Under these circumstances the glomerulus undergoes ischæmic necrosis. The glomerular hæmorrhage seen *post mortem* occurs when the muscular spasm relaxes preceding death. The blockage of the afferent glomerular artery causes a simultaneous stoppage of the blood flow in the efferent glomerular artery, and therefore the tubules suffer from, and are impaired by, similar ischæmia; hence the "nephrotic" syndrome and acute tubular necrosis. Does albumin enter the urine through the excessive permeability

of the glomerulus, or through the excessive permeability of the tubules in the region of Henle's loop, or through both? The prevention of this condition should be based upon the maintenance of adequate blood pressure and adequate hydræmia of the blood. In view of Trueta's experiments with staphylococci toxin, it is likely that the hypothesis also has a bearing upon the ætiology of acute nephritis.

Preeclampsia.

From histories given by his patients with preeclampsia and eclampsia, Kelsall believes that the seeds of toxæmia are often sown early in pregnancy by the patient's ingestion of large quantities of sodium antacid mixtures for indigestion and nausea. The work of Loeb suggests that the substitution of potassium for sodium in all drugs taken by the patient would act as a prophylactic against toxæmia and eclampsia.

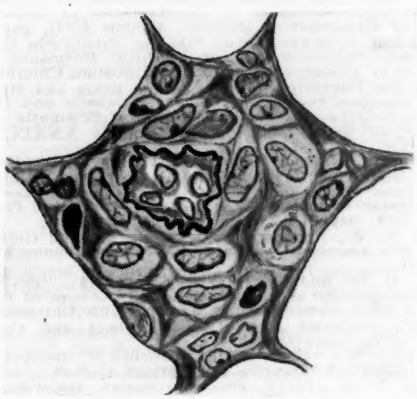

FIGURE V.

After Zimmermann. Bat kidney, fixed with Tellyesniczky formol injection, Azan stain. Both arteries are cut longitudinally. In the wall of the afferent artery (arising from the bottom of the illustration) there is a weakly developed "pole-cushion". The connexion of its cells with the muscle fibres is obvious. The endothelial nuclei of the afferent artery show their pronounced "tearlike" shape with their broad end towards the glomerulus. The efferent artery, which is in the top left-hand corner, does not show this. The *macula densa* of the distal convoluted tubule is situated on the left between these two arteries. Note the muscle fibres surrounding the *macula densa* and forming a sphincter to it. It can be seen that the contraction of the muscle scaffolding of the juxtaglomerular apparatus will constrict both the afferent artery and the distal convoluted tubule. (× 1066.)

Our knowledge that an ischæmic organ produces a vasopressor substance suggests the explanation of why bed-rest is so effective in the earlier stages of preeclampsia. Preeclampsia occurs in those patients whose vascular system is unable to satisfy both the needs of the patient's own body and those of her pregnant uterus. Any exercise diverts blood to the muscles exercised, and hence tends to direct it from the uterus. The uterus, thus deprived of adequate blood, initiates the compensatory mechanism of hypertension in order to increase the total blood flow through the body. If the patient is rested at a sufficiently early period this hypertension can often be alleviated.

GENERAL CONCLUSIONS ARISING FROM THE ARGUMENTS PUT FORWARD IN MY TWO PAPERS.

We may now attribute symptoms appearing in pregnancy, preeclampsia and eclampsia to the following causes.

Normal Physiological Changes in Pregnancy.

Water and electrolyte retention produces an increase in the patient's weight over and above that of the fœtus and maternal reproductive organs. The cause is an increase in the intracellular sodium : potassium ratio and in the extracellular electrolytes under the action of progesterone and desoxycorticosterone, which are themselves activated by chorionic gonadotrophin.

Preeclampsia.

The signs and symptoms of preeclampsia are as follows.

1. *Hypertension.*—Hypertension is a compensatory phenomenon, which ensures that every vital organ in the body receives an adequate blood supply. It can be produced through neural and humoral mechanisms. In pregnancy it is the hormone of the posterior lobe of the pituitary which is of special importance in maintaining a raised pressure. The sudden rise of blood pressure in eclampsia is probably a neural and osmotic effect which will be discussed later.

2. *Albuminuria.*—Under the action of the posterior pituitary principle, the juxta-glomerular body goes into spasm and prevents an adequate blood supply to the glomerulus. Hence, the cells of the glomerulus are damaged and their permeability is temporarily increased from anoxia. When the spasm of the juxta-glomerular body relaxes, the glomerular capillary membrane passes albumin into the filtrate.

3. *Œdema.*—Œdema of gradual onset is an exaggeration of the water retention of normal pregnancy, the excess fluid accumulating in the tissue spaces. The nature of œdema appearing suddenly in connexion with eclamptic convulsions is explained later.

Eclampsia.

The signs and symptoms of eclampsia are eclamptic convulsions, rapidly occurring hypertension and œdema.

In my previous paper on this subject I pointed out that the tissue œdema and fall of plasma proteins which preceded eclampsia were likely to produce relative anoxia and acidosis in the environment of the cells; this would prove toxic to the cells and in particular would make the functional cells of the nervous system, the neurons, more irritable. However, this hypothesis requires elaboration in the light of the membrane theory (Bernstein) of nervous conduction. According to this theory, conduction is a surface phenomenon. The nerve fibre is surrounded by a semi-permeable membrane, which is polarized when the nerve is at rest. Thus, the membrane separates a layer of internal kations from a layer of external anions. Hence, a nervous impulse is initiated by an increase in the permeability of the membrane at the point of stimulation (local excitatory state). This results in a temporary exodus of the kations so that the membrane becomes depolarized. At the point of stimulation, therefore, the nerve becomes relatively negative to the section of nerve immediately adjacent to it, and a potential difference is created between these two sections of nerve. A current passes and the adjacent portion of nerve is also depolarized. Thus, a wave proceeds along the nerve fibre which constitutes the nervous impulse. The neuron remains refractory until the membrane becomes repolarized.

Now, the basis of the argument presented in these two papers is that some steroid hormones can cause an alteration in the constitution of the kations on the internal side of the cell membrane, which increases the osmotic pressure (that is, potential difference) across the membrane. If the internal kations are exerting a pressure on the extracellular fluid, tending to attract water inwards from the extracellular fluid, it follows from physical laws that the extracellular fluid is tending to force the kations outwards. This tendency is diminished under influence of the steroid hormones. This is identical to stating that the steroid hormones make the cell membrane less permeable to the exodus of the intracellular kations.

While the activity of the steroid hormones is increasing all is well with the patient, because the increase of intracellular sodium ion goes hand in hand with an increasing impermeability of the membrane. To put the same process in other words, the nerve cell is becoming simultaneously

more "fully-charged" and less irritable per unit of charge. Hence, no physiological activity takes place. However, during the last few weeks of pregnancy the secretion of chorionic gonadotrophin decreases. This decrease is accompanied by an even more pronounced decrease in the secretion of the steroid hormones. This is the critical danger period, in which we have an "over-charged" nerve cell with an ever-increasing permeability of the cell membrane, and hence an ever-increasing irritability. Thus, we may expect even in the normal pregnant woman that a diminution of the secretion of the placental hormones will be accompanied by an increased irritability of the nerve and muscle cells of the body.

Of course, in the normal patient, as the steroid hormone activity is reduced, the neuron discharges its excess kationic potential gradually, and the local excitatory state does not approach the threshold value for a spontaneous impulse. However, in the preeclamptic the "over-charge" may be great and the withdrawal of steroid hormone rapid. In such instances the neurons of the motor cortex may reach such a degree of irritability that the arrival of strong afferent impulses to brain sets up a mass discharge of the motor neurons—that is, eclamptic convulsions.

The stimulation of the muscle fibres during these convulsions accelerates the release of the "over-charge" of the muscle cells. Hence, there is a sudden increase in the kation concentration of the extracellular fluid. This release of kation has two effects. (i) As shown by Verney, it stimulates the release of the posterior pituitary principle with its corresponding suppression of urine and rise of blood pressure. (ii) It releases into the circulation intracellular fluid, retained intracellularly by osmosis. This fluid is then deposited in the tissues and appears suddenly as œdema.

The great advantage of this hypothesis, which proposes that eclampsia appears as a withdrawal symptom, is that it explains the phenomenon of post-partum eclampsia as well as the occasionally sudden appearance of fits, hypertension and œdema in an apparently healthy pregnant woman. It will thus be seen that this hypothesis has been developed to a point at which it can account for all the salient signs and symptoms of "toxæmia of pregnancy".

SUMMARY.

Clinical and experimental work bearing on the pathological mechanisms giving rise to eclamptic convulsions is correlated. The chorionic hormone of the placenta stimulates the activity of the steroid hormones of the adrenal gland and *corpus luteum*, which together with the placental hormones cause an increase in the intracellular sodium-potassium ratio. This increases the osmotic pressure of both intracellular and extracellular fluids. Verney has shown that an increase in the osmotic pressure of the extracellular fluid stimulates the antidiuretic action of the posterior pituitary body. The antidiuretic hormone increases the tone of the juxta-glomerular body, which acts both as a sphincter to the renal tubules and as a clamp to the afferent glomerular artery. This hypothesis thus accounts for the hypertension, albuminuria (through ischæmic impairment of the glomerulus) and œdema of preeclampsia.

Reasons are given for believing that the neuro-muscular system becomes highly irritable during the stage of withdrawal of the placental hormones, and the excitatory state of this system may become sufficiently great to culminate in convulsions.

The hypothesis is correlated also with the pathology of acute cortical necrosis and acute nephritis.

ACKNOWLEDGEMENT.

I am greatly indebted to Dr. T. R. Lubbe for his translation from the German text, and to Mr. A. C. Waldon, who reproduced the illustrations for me from the original sources.

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THE "KINK" IN THE AORTA.

By J. B. CLELAND, C.B.E., M.D.,

Emeritus Professor of Pathology, University of Adelaide.

FOR many years now it has been my custom when performing autopsies to measure the size of the aorta first above the aortic valve and again just above the diaphragm by means of brass cones, kindly prepared and calibrated by Dr. H. M. Birch. The aorta, it may be mentioned, increases in calibre with age (Cleland, 1936) and the size may be of value in determining approximately the age of an unknown person or in checking the supposed known age, as some people look younger or older than they are. In cutting a ring of the ascending aorta for measuring purposes, it is necessary to avoid being too close to the valve and injuring it on the one hand, or too near the arch of the aorta on the other hand, because the curve of the arch would vitiate the reading. When the pericardium is opened and the aorta inspected, an appearance is seen on the right side of the outer aspect of this vessel and just about the commencement of the arch, which gives the impression that there is here a kink in the vessel. When the vessel is opened it is of course seen that no such kink is present. What gives the impression of such a kink on the outside is a fold of connective tissue, in which varying amounts of adipose tissue may be deposited. In fat and well-covered bodies the amount present may cause a prominent fold to appear, but in emaciated persons the loose ring of tissue may not be very obvious. Longitudinal sections examined microscopically show in suitable cases considerable fat in the fold, the periaortic tissues proximally and distally being closely applied to the wall and without adipose tissue, at least

in appreciable amount. The fold can be seen in well-nourished new-born infants and in children as well as in adults. It is situated about 2·7 to 3·7 centimetres above the pericardial reflexion onto the commencement of the aorta. I presume it has some developmental significance, but my anatomical friends can give me no information on this point.

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Reports of Cases.

REPORT OF A CASE OF ACUTE RHEUMATIC FEVER TREATED WITH CORTISONE.

By B. McC. O'BRIEN, B.Sc., M.B., B.S.,

AND

J. T. CAHILL, M.D., M.R.C.P., M.R.A.C.P.,

Saint Vincent's Hospital, Melbourne.

IN acute rheumatic fever it is a well-known fact that joint symptoms and pyrexia in the great majority of cases are controlled by the adequate oral administration of salicylates. However, it is extremely doubtful whether salicylates influence the course of rheumatic carditis. It would appear, therefore, that any drug that could control all the features of rheumatic fever would be a most valuable therapeutic agent. From recent work it would seem likely that cortisone is such an agent, although no conclusive evidence or long-term results are available to indicate that it does prevent cardiac damage.

The case presented is of interest because of the total lack of response to salicylates, the severity of the cardiac damage during a recurrent attack of rheumatic fever, and the response to cortisone.

Clinical Record.

W.W., a single man, aged thirty-four years, was admitted to Saint Vincent's Hospital, Melbourne, on December 30, 1950. He had suffered four previous attacks of acute rheumatic fever, the last being in 1938, after which no residual cardiac damage was discovered. Three weeks before his admission to hospital he complained of a sore throat, which was followed two weeks later by a typical attack of acute rheumatic fever with joint involvement. Examination confirmed the joint features and revealed a temperature of 102·4° F., tachycardia with regular rhythm, and an apex beat four and a half inches from the mid-sternal line in the fifth left intercostal space. The blood pressure was 120 millimetres of mercury, systolic, and 80 millimetres, diastolic. No skin nodules were detected. Salicylate therapy (20 grains every three hours initially, then every four hours) was instituted, but no response was obtained. The dosage was increased to 30 grains every three hours after thirteen days, but still no effective response was forthcoming.

At this stage a number of investigations had been carried out with the following results. The urine was normal on microscopic examination. An X-ray film of the chest was normal. An attempt at blood culture gave negative results. The red blood cell count was 3,890,000 per cubic millimetre, the leucocyte count was 19,320 per cubic millimetre, the hæmoglobin value was 72%, the colour index was 0·9, and the blood sedimentation rate was 120 millimetres in the first hour. The plasma protein content was 6·5 grammes *per centum* and the albumin-globulin ratio was 1:1.

Approximately two weeks after the patient's admission to hospital gallop rhythm appeared at the apical area, and on January 16 he became very ill. His temperature rose further, the joint symptoms worsened, the pulse rate was 140 per minute, severe dyspnœa occurred, pericardial and pleuro-pericardial friction rubs became evident, bilateral rheumatic pleurisy with very prominent pleural friction rubs appeared, and the apex beat moved out to five and a half inches from the mid-sternal line in the fifth left intercostal space. No features of a pericardial effusion were present, nor were any signs of congestive cardiac failure evident at this stage. The joints involved included ankles, knees, wrists, shoulders, elbows and all metacarpophalangeal and proximal interphalangeal joints—in other words, both large and small joints were affected, though not all simultaneously.

As there had been no response to sodium salicylate therapy despite apparently adequate dosage, it was discontinued and the administration of cortisone acetate was commenced on January 16. The initial dosage was 100 milligrammes given intramuscularly twice a day for the first two days, and then a daily dose of 100 milligrammes given intramuscularly.

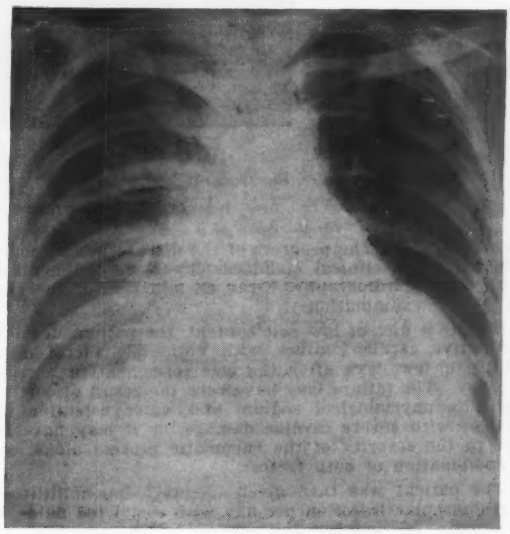

FIGURE I.

X-ray film taken on January 19, three days after the commencement of cortisone therapy. It shows an enlarged heart and loss of translucency in both lungs, particularly the right.

Further investigations were carried out before the cortisone was used. The blood urea content was 45 milligrammes *per centum*; the serum potassium and blood cholesterol and glucose contents were all within normal limits. X-ray examination of the chest on January 19 showed the heart still enlarged and there was a loss of translucency in both lungs, and particularly the right, suggesting some pulmonary inflammation. An electrocardiogram revealed sinus rhythm with a *P-R* interval of 0·2 second.

Within thirty-six hours of the commencement of cortisone therapy there was a dramatic fall of the temperature to normal, dyspnœa disappeared, joint symptoms lessened considerably, and range of movements became much greater. The patient felt much improved, the heart size decreased, the gallop rhythm disappeared for several days, the apical rate dropped to 90 per minute, and the pericardial friction rub disappeared (Figure I).

From the beginning of the cortisone treatment the daily fluid intake and output were recorded, a low salt diet was given and the urine was tested twice a day for sugar and ketone bodies. An electrocardiogram on January 19 (Figure II) revealed sinus rhythm, flattened *T* waves in lead I, and inverted *T* waves in all precordial leads. Serum potassium estimation on this day was normal.

Repeated investigations were carried out to determine (i) any side reactions to the use of cortisone, and (ii) the

progress of the disease. The first group (side reactions) covered sodium and water retention, potassium deficiency, alterations in blood pressure, glycosuria, hyperglycæmia, cholesterolæmia and hormonal disturbances — that is, features of Cushing's syndrome. Blood sugar estimations were performed twice a week and the blood pressure was recorded daily. The progress of the disease was measured, other than by clinical standards, by blood sedimentation rate, electrocardiography, X-ray examination of the chest, and blood examination.

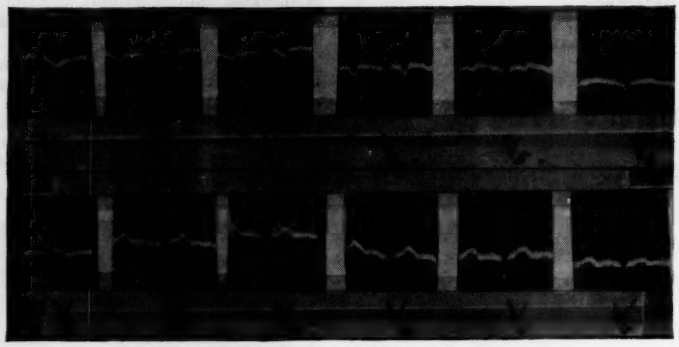

FIGURE II.

Electrocardiograms. Series I: January 19 (three days of cortisone therapy); all precordial leads show inverted *T* waves. Series II: January 25 (nine days of cortisone therapy); *T* waves upright.

Despite a diet of low salt content, the patient developed congestive cardiac failure with noticeable sacral œdema within a few days after the commencement of cortisone therapy. The failure may have been the result of cortisone with its physiological sodium and water retention in a patient with severe cardiac damage, or it may have been due to the severity of the rheumatic process alone, or to a combination of both factors.

The patient was then given "Neptal", one millilitre by intramuscular injection per day with restricted fluids, and gradually the œdema disappeared. The patient's facial characteristics changed within a week of cortisone therapy, a change which may have resembled the full-moon appearance reported with the use of cortisone. Clinically or with the aid of investigations no side reactions were definitely determined.

After a temporary disappearance of several days, gallop rhythm and pericardial friction rub returned. However, by January 28, after twelve days of cortisone therapy, joint movements were painless and normal in range, and there was no congestive cardiac failure, gallop rhythm, pericardial friction rub or pleural friction rub. The pulse rate ranged from 90 to 100 per minute, the temperature was normal and the apex beat was three and a half inches from the mid-sternal line in the fourth left intercostal space. At this stage the electrocardiogram (Figure II) showed *T* waves upright in all leads, the blood sedimentation rate had fallen considerably, and from the X-ray film of the chest the heart was normal in size and the lung fields were clear.

The cortisone dosage of 100 milligrammes per day was continued to January 26 (ten days' therapy), when, owing to limited supplies, the dosage was reduced to 50 milligrammes per day. (Figure III shows the X-ray appearances in the chest on January 30.) On January 31 joint pains reappeared, the temperature rose to 102° F., the pulse rate became 130 per minute, and gallop rhythm returned. The dosage of cortisone was increased to 100 milligrammes per day. Again within thirty-six hours the attack subsided except for a mild tachycardia and gallop rhythm, which persisted for about one week after the first course of cortisone terminated on February 6, when 2·1 grammes had been given. The blood picture had improved by this time; the red blood cell count was 4,620,000 per cubic millimetre, the white blood cell count was 22,640 per cubic millimetre, the hæmoglobin value was 90%, the colour index was 1·0, and the findings in a differential leucocyte count and blood smear were normal. An electrocardiogram showed the *P-R* interval to be just over 0·2 second.

With cessation of cortisone therapy, the administration of "Neptal" was discontinued. It was thought that, rather than jeopardize the patient's chances, salicylate therapy (20 grains every four hours) should be recommenced in the hope of preventing a recrudescence of his joint symptoms and pyrexia.

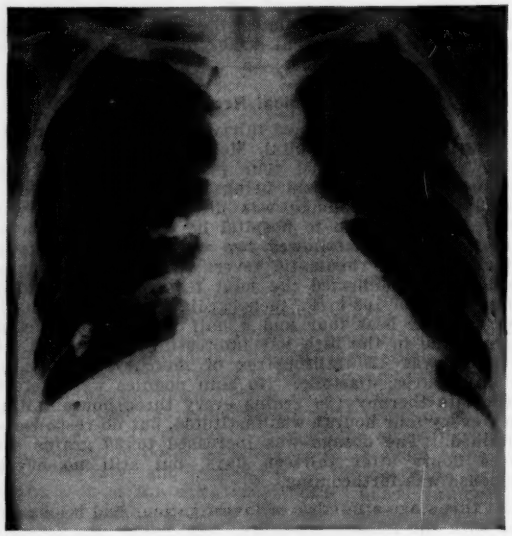

FIGURE III.

X-ray film taken on January 30, after two weeks of cortisone therapy. The heart size is considerably less and the lung fields have cleared. The opaque area in the lower right lung field is a button on the patient's clothing.

Another flare-up of the rheumatic fever occurred two weeks after the termination of the first course of cortisone therapy, with further evidence of myocardial involvement. No effect was again obtained with salicylates. A second course of cortisone with a daily dosage of 100 milligrammes was commenced on February 24, salicylate therapy being discontinued. An effective response was obtained, the

patient being afebrile within two days. A course of one gramme was given. The pattern of response was similar to the first course—rapid disappearance of fever and joint symptoms, slower response of the cardio-vascular signs. The second course terminated on March 6.

Two weeks after the final cessation of cortisone therapy tachycardia had disappeared, the temperature was normal, no cardiac irregularities were present, the heart was slightly enlarged, the blood sedimentation rate was seven millimetres in the first hour, and the electrocardiogram was within normal limits. Salicylates were given again after the second course of cortisone.

toms in thirty-six hours. (ii) The slower response of the cardiac disorders. The electrocardiogram became normal after about one month. The fall in pulse rate was not rapid. (iii) The minimal effective dosage of 100 milligrammes per day. This was demonstrated by the flare-up on a reduced dosage of 50 milligrammes per day and control of the condition by a subsequent increase to 100 milligrammes per day. The initial dosage in this case was 200 milligrammes per day (divided dose) for two days, but this could not be maintained owing to short supply. With this patient two courses of three weeks' and ten days' duration respectively were given, these times being judged

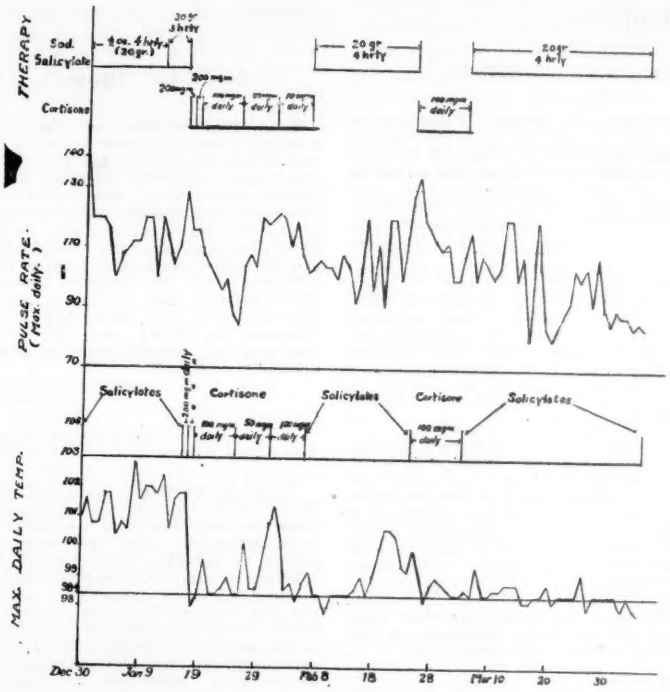

FIGURE IV.
Graph showing changes in temperature and pulse rate following the use of salicylates and cortisone.

The patient was discharged to the convalescent home on April 5, quite well.

Reexamination of the patient on May 21 showed that improvement had been maintained; he had no dyspnœa on exertion, had gained nine pounds in weight since his discharge from hospital, and had a good appetite. The apex beat was located in the fourth left intercostal space four inches from the mid-sternal line, and mild tachycardia was present. Further investigations gave the following results. The electrocardiogram was normal. The blood sedimentation rate was 10 millimetres in the first hour. The red blood cell count was 5,160,000 per cubic millimetre, the white blood cell count was 8600 per cubic millimetre, the hæmoglobin value was 100%, and a differential leucocyte count and examination of a blood smear gave normal results. Fluoroscopic examination of the heart gave normal results.

Discussion.

It was believed that cortisone saved this man's life, as his condition was deteriorating rapidly despite high dosages of salicylates. (The effects of salicylate and cortisone therapy are shown graphically in Figure IV.)

Features of the use of cortisone in this case were as follows. (i) The rapid response of fever and joint symptoms by the activity of the disease. Careful use of cortisone with adequate biochemical control would seem advisable. (iv) The superiority of cortisone over salicylates. (v) The return of the red cell count and hæmoglobin value to normal in three weeks.

Cortisone is not without risk in cardiac cases. It is possible that the congestive cardiac failure in this patient may have followed the use of cortisone, though the severity of the myocarditis alone may have been responsible.

It is not known whether cortisone will invariably prevent cardiac damage, but it seems reasonable to expect that its immediate use in any attack, and particularly the first, will reduce the incidence of cardiac involvement. Only a long follow-up can reveal the relationship between cortisone therapy and the prevention and control of cardiac damage.

Summary.

A case of recurrent acute rheumatic fever with severe cardiac and joint involvement and bilateral rheumatic pleurisy treated with salicylates and cortisone is described. The recovery of the patient is outlined. The dosage and toxic effects of cortisone are discussed. Whilst no wide conclusions can be drawn from one case, it would appear that severe rheumatic fever may be the most important

justifiable indication for the use of cortisone while the latter is in short supply.

Acknowledgement.

We wish to acknowledge the kind permission of Dr. T. A. F. Heale to publish this case and to thank him for his helpful advice. Our thanks are due to Mr. P. Sullivan, of the hospital photographic department, and to the staff of the records department, for their assistance in the preparation of material.

Reviews.

CARDIOLOGICAL INVESTIGATIONS.

"The Practical Significance of Modern Cardiological Investigations" by Lowe, Kay and Luke is a monograph which won the Stawell Memorial Prize for 1949.[1] It is based on personal observations supplemented from the available literature, and is divided into three parts which deal with (*a*) the techniques in detail, their use and their reliability; (*b*) the cardiac conditions in which the investigations are most necessary; and (*c*) circumstances in which they are more or less incidental.

This book should be read for what it is and not as a synopsis of cardiology. Since it was written further advances have been made in some of the methods described, including the recording of intracardiac pressures by multichannel apparatus, one of the authors' hopes being thus fulfilled. The authors mention venous spasm in catheterization, a difficulty which Paul Wood strongly asserts can usually be avoided by adequate local anæsthetization and the choice of a catheter not too large for the vein.

There are a number of misprints, and the *P-R* interval is stated to be the longest interval in any of the limb leads, whereas White points out that it should be the shortest one. Mention is made of Piesch's placing much weight on myocardial as opposed to valvular lesions, but the pendulum is now swinging back to allow the surgeons to attack mitral and aortic stenosis. The authors obviously have a good knowledge of their subject and its literature, as is shown by their most useful references. They are also to be complimented on the excellent illustrations, although the group insertion is not ideal. Knowing the sound practical work they have done, the reader will be rather disappointed that there is not more reference to their own experience.

TETANUS.

A young Italian, Mario Pelloja, clinician and researcher, has devoted much study and investigation to the problems of the tetanus bacillus, the effects of its toxin, the nature of antitoxin and the methods of treatment including active and passive immunity. His book, *"Le tétanos expérimental par la toxine tétanique"*, is not described as a university thesis and has none of the faults, such as padding, which such efforts all too frequently display.[2] The bibliography includes some 1300 references, and perusal of the book will convince the reader that this formidable list has not arisen from expert librarianship, but that the articles cited have been read and assimilated. The book begins with the culture of the bacillus and then deals in detail with the characteristics of the toxin and its effects on every imaginable sort of tissue. His many personal researches have convinced the author that the tetanus bacillus does not travel centripetally by the nerve trunk or by perineural lymphatics, but simply in the blood-stream, and the presentation of the evidence will carry conviction. The cause of the incubation period is discussed with admirable clarity. As no other toxin has been investigated with so much care and attention to precise quantitative measurements such as titration with antitoxin and the binding powers of various tissues in various animals, it might be thought that little remained to be added. A study of this book shows clearly that such is not the case. Here problem after problem is revealed and some are satisfactorily unravelled. The author is a skilled and tireless investigator, but above all he is a clinician, and the several methods of combating the tetanic convulsions, apart from serum therapy, are analysed in all their complexities and guidance is given to the physician and surgeon. Seldom in recent medical history have the pathology and therapeutics of a microbal invasion been presented with such comprehensiveness and with such soundness of judgement. A preface by Dr. Rondoni, Director of the Institute of General Pathology in Milan, pays a generous tribute to the young author and to the help proffered by French colleagues and publisher.

BIOLOGICAL THERAPY AND PROPHYLAXIS.

That two editions of Parish's "Bacterial and Virus Diseases" have appeared within three years is the best indication that this short vade-mecum meets a real need.[1] The book, which in size and scope is comparable to the "pocket-prescribers", gives clear and concise information on the realm and limitations of biological therapy and prophylaxis. The short introduction states in simple language the basic immunological concepts, whilst the further chapters are arranged according to the various types of biological products such as antisera, preparations used for active immunization and diagnostic reagents. To those practitioners who are interested in preventive medicine the chapters on B.C.G. and the vole bacillus and the two chapters on immunization against virus diseases will be specially welcome.

CURRENT THERAPY.

"Current Therapy" appeared first in 1949 and again in 1950. Both editions were reviewed in this journal. The form of the book and its editor's aims and achievement were discussed. The 1951 edition is now available.[2] The editor, as before, is Dr. Howard F. Conn, who has a large number of eminent contributors as well as a panel of consulting editors to help him. Each contributor clearly sets out the regimen in current use in his clinic. It is known as his "method", without, of course, any suggestion that he is the originator of the method. As well as medical, important surgical, obstetrical, gynæcological and skin conditions are covered. Although each contributor is necessarily dogmatic, the reader often has a chance of comparing the methods of more than one authority for a particular condition. Vague hints and pronouncements, often a source of irritation in some works, are with few exceptions absent. One is rarely left in doubt as to dosage and application of the many drugs in use. A "roster of drugs" forms a very useful appendix. Nevertheless, a critical spirit is still needed. The reader would do well, for example, to satisfy himself as to the safety, solution and dilution of certain drugs which he is just told to give intravenously.

In the preface it is stated that forty-nine new contributors have been added since the 1950 edition, and eighty-six of the methods are new. No details of these changes are given in the preface, nor can they be given here. A much fuller account is given of the newer antibiotics. We note also a more satisfying description of the treatment of all forms of meningitis than we did before. A number of other drugs are, from increased experience, more confidently recommended.

For quick and ready reference to notable authorities the practitioner will find this book most useful. We can hardly, however, recommend its annual purchase. Much must appear again that has gone before. The book is expensive to buy every year; and it is bulky, even if the large double-column type is a delight to read.

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[1] "The Practical Significance of Modern Cardiological Investigations", by T. E. Lowe, M.D., D.Sc., F.R.A.C.P., M.R.C.P. (London), H. B. Kay, M.D., M.R.C.P. (London), M.R.A.C.P., and H. A. Luke, M.B., B.S., D.D.R.; 1951. Melbourne: Melbourne University Press. 9" x 6", pp. 206, with 47 plates and 13 diagrams. Price: 45s.

[2] *"Le tétanos expérimental par la toxine tétanique"*, by Mario Pelloja; 1951. Paris: Masson et Cie. 10" x 6¼", pp. 300, with illustrations. Price: 1000 fr.

[1] "Bacterial and Virus Diseases: Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment", by H. J. Parish, M.D., F.R.C.P.E., D.P.H.; Second Edition; 1951. Edinburgh: E. and S. Livingstone, Limited. 7½" x 5", pp. 212, with about 20 illustrations. Price: 10s. 6d.

[2] "Current Therapy 1951: Latest Approved Methods of Treatment for the Practicing Physician", edited by Howard F. Conn, M.D.; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 11" x 8", pp. 730. Price: £4 15s.

The Medical Journal of Australia

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PENICILLIN AND THE PREVENTION OF ACUTE RHEUMATIC FEVER.

THE remarkable developments of the past fifteen years in the control of acute infections, first by the sulphonamides and then by the antibiotics, have brought hope to those who are concerned with the crippling sequelæ of acute rheumatic fever. Many reports have appeared on the role of the sulphonamides in the prevention of acute rheumatic fever, and there is widespread confidence in their worth. Critics are not lacking, and they have found good grounds for their criticism, especially in some of the more sweeping claims based on inadequately controlled investigations. Nevertheless, we cannot lightly dismiss the favourable findings from such careful work as that reported from Melbourne in 1949 by S. D. Rubbo, M. C. Holmes and H. L. Stokes[1] (see THE MEDICAL JOURNAL OF AUSTRALIA, October 1, 1949, page 511). Unfortunately the sulphonamides have their own peculiar disadvantages which apply in this as in every other field of their application, and a strong tendency exists to discard them from therapeutics whenever a less troublesome agent will achieve the same desired effect. It was inevitable, then, that penicillin should be considered as a prophylactic agent against rheumatic fever. In 1948 B. F. Massell *et alii*[2] reported the results of a small investigation. Orally administered penicillin in doses of 300,000 to 1,000,000 units per day for ten days suppressed hæmolytic streptococci in all but 2·1% of 235 cultures prepared from throat swabbings of 37 patients with rheumatic fever. It completely eradicated the organisms from the throats of 28 of the 37 patients. The reduction in streptococcus carrier rate by penicillin therapy and the prompt treatment of hæmolytic streptococcal infections with penicillin did not completely prevent the spread of streptococcal infections among ward patients. Massell and his colleagues were encouraged by their results to suggest that prevention of hæmolytic streptococcal infections and so rheumatic fever prophylaxis might be practicable with penicillin. Their paper was read at an American Medical Association meeting, and according to the short reported discussion seems to have been received cautiously.

In January, 1949, an investigation of major proportions was begun at Francis E. Warren Air Force Base in south-eastern Wyoming, having as its subject the prevention of rheumatic fever by the prompt treatment of streptococcal infections with penicillin. The base is an air force technical training centre with an average strength during the period of the study of 8000 men. The actual number of men exposed to infection was much greater since the population is moving; the average turnover is 1000 men per month. All soldiers reporting sick with respiratory symptoms who had either exudative tonsillitis or pharyngitis or an oral temperature of 100° F. or greater were admitted to hospital. Within a few hours of admission to hospital each patient was examined by a member of the professional staff of the laboratory, and blood for a leucocyte count, a swabbing of the tonsils and oropharynx for culture and a specimen of serum were obtained. A standardized history and physical examination were used. Only patients with exudative lesions on the tonsils or oropharynx were included in the study group. Those with an air force serial number ending in an even digit were treated by intramuscular injection of crystalline procaine penicillin G in peanut or sesame oil containing 2% of aluminium monostearate. Those with a serial number ending in an odd digit received no specific treatment and served as controls. Three different dosage schedules were used. A careful follow-up was made for the detection of rheumatic fever. A preliminary report of this investigation was published last year by F. W. Denny, L. W. Wannamaker, W. R. Brink, C. H. Rammelkamp and E. A. Custer,[1] covering groups of 798 treated patients and 804 untreated patients. Rheumatic fever had been developed by two of the treated patients and by 17 of the control group, and it was claimed that the data presented established the fact that penicillin therapy for acute streptococcal infections will almost completely prevent the development of rheumatic fever.

A further report has now been published on the investigation at Francis E. Warren Air Force Base, this time by Wannamaker, Rammelkamp, Denny and Brink with H. B. Houser, E. O. Hahn and J. H. Dingle.[2] It is a comprehensive report that must command general attention. The numbers in the treated and untreated groups are now increased to 1178 and 1162 respectively. Ten of the treated patients and 42 of the controls developed an illness classified as definite or possible rheumatic fever. However, data collected on rheumatic subjects showed that reinfection with a new type of streptococcus frequently occurred when the interval was prolonged between the onset of the observed attack of exudative tonsillitis and the onset of rheumatic fever. As penicillin therapy could not be expected to prevent rheumatic fever when an intervening streptococcal infection was not treated with the

[1] *The Lancet*, August 20, 1949.
[2] *The Journal of the American Medical Association*, December 4, 1948.

[1] *The Journal of the American Medical Association*, May 13 1950.
[2] *The American Journal of Medicine*, June, 1951.

drug, all patients who developed rheumatic fever after forty-five days from the onset of the observed illness were excluded for the purposes of discussion in this study. On this basis there were only two definite cases of rheumatic fever among patients treated with penicillin and 28 cases among those in the control group. This difference in incidence is claimed to be, and certainly appears to be, highly significant. Penicillin therapy was also found to eradicate the streptococcus from the oropharynx of the majority of infected persons and to inhibit the formation of antistreptolysin. The greatest inhibition of antibody resulted from three injections of penicillin given over a period of ninety-six hours and totalling 1,200,000 units; the effect was greater than that from either a single injection of 600,000 units or two injections of 300,000 units each, given seventy-two hours apart. Wannamaker and his colleagues quote evidence which suggests but does not establish that eradication of the streptococcus itself from the throat is not necessarily related to the prevention of rheumatic fever. It would appear, on the other hand, that the ideal form of preventive therapy would be that which inhibited antibody production to the maximum degree. Sulphonamides only slightly inhibit antibody production. Aureomycin has a considerable inhibitory effect, and also decreases the number of organisms, and its use may result in a diminished incidence of rheumatic fever. Penicillin administration results in the eradication of the streptococcus, a reduction in antibody production and a decrease in the incidence of rheumatic fever.

It is to be hoped that this work will receive wide attention and that practitioners will carry out carefully controlled check investigations for themselves. As Wannamaker and his colleagues point out, the recognition of streptococcal infections is important, and they claim that it may be done without the employment of complicated laboratory procedures. We quote their criteria. The illnesses are characterized by the sudden onset of sore throat (with soreness on swallowing), which is usually associated with constitutional reactions. Streptococcal respiratory infections, in contrast to many non-bacterial respiratory infections, are attended by a considerable rise in temperature. The development of symptoms and fever usually reaches a maximum degree about twenty-four hours after the onset. The physical sign regarded as especially helpful in diagnosis is the presence of enlarged and tender cervical lymph nodes. The pharynx is diffusely injected, the lymphoid tissues and the soft palate appear œdematous, and exudative lesions are common. If the diagnosis is doubtful a leucocyte count should be obtained; if the number is 10,000 per cubic millimetre or more, the infection should be considered streptococcal in origin until proven otherwise. Occasionally culture of material from the throat is required. It is suggested that depot penicillin may be used in the dosages outlined in schedule I of the reported study (300,000 units *statim*, 300,000 units at the end of forty-eight hours, 600,000 units at the end of ninety-six hours), or perhaps two injections of 600,000 units may be given at an interval of seventy-two hours. The sodium salt in doses of 15,000 to 25,000 units every three hours for eight to ten days may be used for patients with a past history of rheumatic fever, because the incidence of recurrent rheumatic fever in such groups is high and such a schedule of treatment appears to be most effective in inhibiting antibody formation.

The general adoption of these recommendations would naturally increase the incidence of penicillin therapy—in many cases for conditions that are apparently minor in degree of severity and likely to subside with simple treatment. This superficially cuts across the advice generally given that heroic measures should not be used when simpler treatment will deal with the situation, and no doubt further evaluation is desirable of the penicillin prophylaxis of rheumatic fever. Nevertheless the results obtained by Wannamaker *et alii* are sufficiently impressive to warrant at least provisional acceptance. Rheumatic fever, especially in the trail it leaves of lifelong crippling cardiac disability, is a scourge of major significance; if, as appears likely, penicillin is an effective prophylactic agent when properly used, this must outweigh many of the otherwise reasonable objections to its lavish use. Much is being done, and promises to be done, in the treatment of the late sequelæ of rheumatic carditis, especially with the rather astonishing development of cardiac surgery; but, as William S. Tillett points out in an editorial comment accompanying the paper by Wannamaker *et alii*, it must be apparent that the greatest contribution to the problems of rheumatic heart disease will and must come from its prevention.

Current Comment.

NOTIFIABLE DISEASES.

In accordance with recommendations made at the thirtieth session of the National Health and Medical Research Council, the table of diseases notified in each State and Territory of Australia, which is published in the journal each week on the last page but one, has been brought into line with a uniform system. The Council's recommendations were as follows: (i) That the following diseases be notified to the Central Health Authority as notifiable diseases for the purpose of information: acute rheumatism (rheumatic fever), brucellosis, chorea (St. Vitus), dengue, encephalitis, filariasis, homologous serum jaundice, hydatid, infective hepatitis, lead poisoning, ophthalmia, rubella, tetanus, trichinosis, typhus (flea-borne, mite-borne and tick-borne). (ii) That the following diseases be notified to the Local Health Authority and the Central Health Authority for statutory preventive measures (this group includes diseases now legally classified as infectious): amœbiasis, ancylostomiasis, anthrax, bilharziasis, cholera, diphtheria, diarrhœa (infantile), dysentery (bacillary), leprosy, leptospirosis, malaria, meningococcal infection, ornithosis, paratyphoid, plague, poliomyelitis, puerperal fever, salmonella infection, scarlet fever, smallpox, trachoma, tuberculosis, typhoid fever, typhus (louse-borne), yellow fever. (iii) That the use of the following terms be discontinued and the alternative title given in parentheses be substituted: cerebro-spinal meningitis (meningococcal infection), enteric fever (typhoid or paratyphoid fever), gastro-enteritis (infantile diarrhœa—to be defined as diarrhœa of more than forty-eight hours' duration in an infant under two years of age), Weil's disease (leptospirosis), Mossman fever and Sarina fever (typhus—mite-borne or tick-borne), psittacosis (ornithosis), puerperal pyrexia and puerperal infection (puerperal fever), scarlatina (scarlet fever), undulant fever (brucellosis). (iv) That notification of the fol-

lowing be discontinued under infectious diseases statutes: beriberi, chickenpox or varicella, coastal fever, *encephalitis lethargica*, erysipelas, favus, helminthiasis, influenza, measles, membranous croup, relapsing fever, scabies, venereal disease, whooping-cough. The list of diseases in the table as it now appears conforms to these recommendations, and it will be understood that the alternative titles adopted have the significance indicated in the Council's third recommendation. Some States of the Commonwealth have already adopted the recommended system. Others must first amend the relevant legislation. It is to be hoped that it will soon come into general use for the sake of desirable clarity and simplicity, as well as the elimination of unsatisfactory or outmoded terminology.

THE PATHOLOGY OF EXERCISE.

THE first of the Lumleian lectures for 1951, delivered by Sir Adolphe Abrahams before the Royal College of Physicians in April of this year, was mentioned recently in these columns. In it certain practical aspects of exercise were considered, more particularly in relation to the healthy person. The subject of the second lecture was the pathology of exercise, and in it Sir Adolphe Abrahams[1] has set himself to examine some of the real or alleged ill effects of exercise, especially in relation to the onset of disease and the aggravation of established bodily disorders. He starts with a reference to death occurring during the performance of physical exertion and notes two features that are as a rule conspicuous: the triviality of the effort, and the discovery of some long preexisting lesion which had never been suspected. When no adequate cause of death is found *post mortem*, Abrahams states, the presumption is the occurrence of an intense vagal inhibition in a strongly predisposed subject, especially of "the more or less hypothetical thymico-lymphatic type"; narrowness of the aorta is a most consistent characteristic. However, after most deaths that occur during exercise, necropsy reveals disease "of such magnitude as to make it almost unbelievable that the sufferer could have survived at all with moderate activity, still less the capacity for outstanding athleticism". Abrahams quotes the post-mortem findings in a number of young athletic subjects when death occurred during mild exercise; these include an enormously dilated right atrium, a patent *foramen ovale* and advanced atheroma of the ascending aorta (all in one subject), coronary atheroma with extensive replacement of the myocardium by fat, congenital absence of the left branch of the coronary artery, and ruptured hydatid cyst of the liver. An outstanding rugby player who died during a strenuous game had fibrotic patches in the wall of the left ventricle, widespread coronary atheroma with narrowing, a very thin soft aorta, advanced hydronephrosis of one kidney and cystic degeneration of the other, and a much enlarged thymus. A Cambridge athlete collapsed after a hurdles race with pain in the back, followed quickly by œdema of the legs and scrotum and more slowly by dilatation of the superficial abdominal wall veins and albuminuria; he died twenty-five years later, when necropsy revealed that the inferior *vena cava* below the hepatic veins was converted into a flat impervious ribbon. Apparently he had, as is often done, held his breath during the race, or most of it, and extreme distension of the inferior *vena cava* had led to localized rupture of the intima followed by forcible extravasation into the walls of the vein whilst exertion was still in progress. An obvious unpredictable hazard of violent exercise is, of course, rupture of a congenital aneurysm.

Referring to exercise and infection, Abrahams rightly draws attention to the danger of exercise during a pyrexial illness, and mentions the association of muscular exercise and certain aspects of poliomyelitis that has had much discussion recently. He is cautious about the relation of exercise to tuberculosis and suggests that the tuberculous diathesis may be accompanied by a flair for athletics; the associated exposure may well be undesirable. One danger of violent exercise not generally appreciated is that of heat stroke, but apparently it is very real. Abrahams mentions in this regard the Marathon race and states that it has so far been held only in countries where great heat is not to be expected. The human body has a remarkable capacity for adjustment, but it seems wise to avoid Marathon running during the hottest hours of the day and under climatic conditions unfavourable to heat loss—a humid atmosphere and a following wind—and in any case the possibility of accompanying hypoglycæmia should be borne in mind. Abrahams refers briefly to the possible role of exercise in the so-called mechanical hypothesis of peptic ulceration, and to the effect of exercise on the nervous system, and he goes on to discuss the relationship of exercise to the kidney, especially in the occurrence of march hæmoglobinuria, the innocent albuminuria of exercise (with its intimate association with the pubertal or postural variety), and the temporary glycosuria that is explained by overflow of adrenaline during exercise. His remarks on "stitch" are interesting, for the nature of this condition is obscure. Theories of its mechanism include stretching of the capsule of the spleen and ischæmia of the diaphragm, but Abrahams considers it to be of ligamentous origin. He points out that stitch occurs in those situations in which the abdominal wall is least able to provide adequate support. When violent jolting movements coincide repeatedly with relaxation of muscles maintaining an intraabdominal pressure and assisting in supporting the viscera, an intermittent tugging occurs on the ligaments supporting the stomach, liver, spleen and bowel. In fact, Abrahams states, the condition is one of acute physiological visceroptosis due to the erect attitude. The use of a tight abdominal binder and care that the stomach is empty before exercise may help, but neither measure is infallible or always acceptable to the athlete. Apparently it must be accepted that stitch results from a special anatomical predisposition that cannot be overcome. Abrahams concludes with a long discussion on "athlete's heart" and on exercise in relation to heart disease.

This is a thoughtful summary by an experienced physician of views that will have wide support, and those concerned with these problems will want to read it for themselves. In brief, Abrahams is not impressed with the possibility of "heart strain" as a sequel to severe physical strain in the absence of previous cardiac disease, and he adopts a common-sense view of the activity legitimate for those with established abnormality or failure of the heart. As pertinent examples of men who avoided unnecessary invalidism he cites John Hunter and James Mackenzie, who lived active, useful lives (and incidentally contributed much to medicine and to mankind) for twenty and seventeen years respectively after myocardial infarction. The attitude adopted towards these cardiac problems is altogether, like much else in these two Lumleian lectures, a refreshing example of mature clinical common sense.

[1] *The Lancet*, June 2, 1951.

JUBILEE OF THE ROYAL VICTORIAN COLLEGE OF NURSING.

THE Royal Victorian College of Nursing is sharing with the Commonwealth of Australia the year of jubilee. Although the college as such came into being only in 1934, it traces its history without interruption from the foundation of the Victorian Trained Nurses' Association in 1901, when Dr. J. W. Springthorpe became the first President. The Association's Royal Charter was granted in 1904. From the beginning a vigorous programme was carried on with considerable success, being aimed always at the development and maintenance of a high standard of nursing and at the care of the best interests of the nursing profession. The Royal Victorian College of Nursing, into which the Association merged in 1934, has continued the successful programme with a growing emphasis on widening educational needs for nurses. The journal of the college, *UNA*, which was started in 1903, has told the full story in a special jubilee issue recently published. The issue is well produced and illustrated and is worth the attention of those who would know more of the history of nursing in Victoria.

Abstracts from Medical Literature.

THERAPEUTICS.

Hodgkin's Disease.

R. GOLDMAN (*The American Journal of the Medical Sciences*, February, 1951) describes the treatment of five patients suffering from Hodgkin's disease with aureomycin. Two to four grammes of aureomycin daily were administered to these patients. In no case was any persisting benefit reported. Subsequently three of the patients were treated with nitrogen mustard with immediate relief.

Oral Cortisone Acetate Therapy.

B. W. BOLAND AND W. E. HEADLY (*The Journal of the American Medical Association*, January 6, 1951) describe oral therapy with cortisone acetate. Twenty-three patients with rheumatoid arthritis were treated, mainly after a course of intramuscular injections, by oral administration of 25 to 100 milligrammes given daily for ninety to one hundred days. Daily intramuscular injection of 20 to 75 milligrammes for one hundred and forty to two hundred days produced great improvement in most cases. Oral treatment yielded as good a response initially, or subsequent to a course of intramuscular treatment. A tablet was given by mouth, usually 300 to 200 milligrammes on the first day, and 100 milligrammes daily thereafter. One patient only out of 23 did not respond.

ACTH and Rheumatoid Arthritis.

H. M. MARGOLIS AND P. S. CAPLAN (*The Journal of the American Medical Association*, February 10, 1951) describe the effects of ACTH on rheumatoid arthritis. They state that 30 to 120 milligrammes of ACTH per day were injected intramuscularly at six-hourly intervals into 56 patients. The patients had suffered from the disease for three to thirty years. Most patients improved. The greatest relief was in cases of early, mild or moderately severe arthritis. Injections at eight-hourly or twelve-hourly intervals were less effective. Relapses developed when the ACTH therapy was stopped, but in mild cases the continuance of a small dose was beneficial. Improvement was less as the drug was continued. Acute infections in these cases were more severe and less well resisted. In four cases severe painful osteoporosis of the spine developed during treatment and was relieved when treatment was stopped. Hypertension developed in six cases, nine patients complained of nervousness, and manifold sociopsychic effects of a serious nature were observed.

Hæmophilus Influenzæ Meningitis.

F. R. MCCRUMB *et alii* (*The Journal of the American Medical Association*, February 17, 1951) discuss the treatment of *Hæmophilus influenzæ* meningitis with "Chloromycetin" (chloramphenicol). They state that aureomycin has been effective in this disorder. Twelve patients were treated with "Chloromycetin" 750 milligrammes followed by 250 milligrammes every four hours by mouth. When vomiting occurred, rectal administration was employed. "Chloromycetin" was given for eight days, the average dose being 10·4 grammes. All patients responded well. Improvement occurred in thirty-six hours, the stiff neck was gone in five days, and fever was absent after two or three days. Blood levels were between five and fifty microgrammes per millilitre. Intravenous dextrose therapy was given uniformly, so that the glucose in the spinal fluid was not a reliable guide to recovery.

Uræmia Complicating Low Salt Treatment of Heart Failure.

A. B. BLACK AND J. A. LITCHFIELD (*The Quarterly Journal of Medicine*, April, 1951) discuss uræmia complicating treatment of heart failure with a diet of low salt content, and refer to eight cases in patients who had been under their care.

ACTH and Peptic Ulcer.

G. A. SMYTH (*The Journal of the American Medical Association*, February 17, 1951) reviews the effects of ACTH on peptic ulcer. He states that it has been claimed that ACTH aggravates peptic ulcer and reports three cases in which there was a recurrence of peptic ulcer during treatment with ACTH. The drug obscured the clinical condition, and one patient died as a result of ruptured ulcer.

"Gantrisin": A New Sulphonamide for Urinary Tract Infections.

B. L. STEWART AND J. J. LASH (*The Journal of Urology*, December, 1950) report on the use of "Gantrisin", a new sulphonamide which has been developed to possess the qualities of wide antibacterial range, together with such solubility that crystallization within the kidney is avoidable. The descriptive formula is 3,4-dimethyl-5-sulphanilamido-isoxazole. It is also called NU-445. The authors present data collected from 100 case studies of urinary tract infection. All the patients in this series were ambulatory and were treated in private practice. They were all very cooperative during the period of observation. Adult patients received four grammes of the drug per day, in four doses of one gramme each, until a total of 25 grammes was given. In most instances only one such course was given, but in nine cases a second course was administered on account of primary failure. Preliminary studies had indicated that high doses were not necessary. Alkalis were not given, but the fluid intake was maintained at 2000 millilitres per day. All patients except those with acute inflammatory lesions had full urological study, and even the latter had their study after the acute stage had subsided. Many of the organic lesions found in this study (calculus, obstructions *et cetera*) made conditions unfavourable from a chemotherapeutic point of view. Nevertheless, such cases were included to show the effectiveness of the drug *in vivo* under conditions which had made infection unresponsive to other sulphonamides, mandelic acid, streptomycin, aureomycin and penicillin. The results indicate that this new sulphonamide is a most powerful agent, widely effective against *Escherichia coli* and most Gram-positive cocci, as well as the notoriously resistant *Proteus vulgaris* and *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*). *Aerobacter aerogenes* was the most resistant organism encountered. However, a good effect was obtained in selected acute cases of infection with this organism. Out of the 100 cases, even with this short course, a total of 67 clinical cures was obtained.

Scleroderma Treated with Cortisone.

M. TAUBENHAUS AND M. LEV (*A.M.A. Archives of Internal Medicine*, April, 1951) describe clinical and histological observations on a patient with scleroderma treated with cortisone. The patient, a woman, aged fifty-two years, gradually developed scleroderma, associated with burning in the fingers and difficulty in swallowing. She was treated with cortisone, 100 milligrammes given every eight hours for one day, then 50 milligrammes every twelve hours until her discharge from hospital after twenty-six days. She improved in relation to the swallowing difficulty. She was cheerful and the skin softened, but there was no return to normal. Skin biopsies revealed thinning of the thickened collagen bundles under the influence of cortisone. The course of the scleroderma was not affected.

J. G. SHARNOFF *et alii* (*The Journal of the American Medical Association*, April 21, 1951) discuss cortisone-treated scleroderma. They state that the patient was reasonably well when treated with cortisone. This treatment gave prompt relief, but later pronounced hypertension and encephalopathy developed, ending with death in uræmia. Others have reported improvement in patients with scleroderma after cortisone and ACTH therapy, but return of symptoms two or three weeks after cessation of treatment. The authors' patient was a woman, aged forty-one years. She was given 300 milligrammes of cortisone on the first day, 200 milligrammes on the second day and 100 milligrammes on subsequent days for some weeks. Within ten weeks the blood pressure rose steadily and renal failure developed with death from uræmia. The authors discuss the relationship of the death to cortisone. They consider that cortisone may well have caused or aggravated vascular lesions of the kidneys giving rise to renal failure and death.

Oral Aureomycin Therapy.

M. MEADS *et alii* (*A.M.A. Archives of Internal Medicine*, April, 1951) describe effects on the bacterial flora of the throat during oral treatment with aureomycin. They state that sulphadiazine, penicillin and streptomycin affect the mouth flora, so that resistant bacteria increase and susceptible ones decrease. These strains of bacteria can be transmitted from one patient to others. Studies suggest that aureomycin is effective against a wider variety of organisms than sulphadiazine or penicillin. Organisms present in the mouth were α and β hæmolytic streptococci, *Hæmophilus influenzæ*, the Neisseria group (Gram-negative cocci), *Staphylococcus aureus* and Monilia. With aureomycin therapy the total number of bacilli in mouth and throat diminished and Gram-negative species become predominant. Aureomycin eliminated *Hæmophilus influenzæ* and coliform species. Pharyngeal strains of α streptococci and Neisseria increased slightly with penicillin, but died out three months after short courses

of aureomycin. Gram-negative bacilli or drug-fast staphylococci also diminished with aureomycin therapy.

Cortisone in Gout.

R. D. FRIEDLANDER (*The Journal of the American Medical Association*, January 6, 1951) quotes a case of acute gout in which clinical improvement followed the use of cortisone, other methods having failed. He states that gout is a disorder of urate metabolism. It may occur without a raised blood uric acid level. The adrenal cortical steroids are believed to be implicated. In the case described there was no response to sodium salicylate or colchicum therapy. Relief followed intramuscular injection of 100 milligrammes of cortisone. This dose was repeated on the two following days, probably unnecessarily. During a recurrence 1/120 grain of colchicine was given thrice daily in addition to 100 milligrammes of cortisone daily for three days with great benefit. Then 20 grains of sodium salicylate given daily and 1/120 grain of colchicine given twice daily kept the patient comfortable.

NEUROLOGY AND PSYCHIATRY.

Desoxyephedrine ("Methedrine") and Electroshock in the Treatment of Depression.

A. B. MUNRO AND H. CONITZER (*The Journal of Mental Science*, October, 1950) have treated 35 depressed patients with "Methedrine" in an attempt to discover whether it is comparable in efficiency with electroshock treatment in cases of depression. The initial dose of 2·5 milligrammes was given before breakfast. Two days later a similar dose was given at noon. Three times a week the dose was increased by 2·5 milligrammes until improvement or side effects occurred. The maximum dose was 30 milligrammes per day in two doses. The blood pressure was measured three times per week. The results indicate that desoxyephedrine is not of equivalent power to electroshock treatment in the treatment of depression. Even when successful it is doubtful whether it is less unpleasant for the patient than electroshock treatment owing to the greater time required to provide relief. There appeared to be about a 50% chance of increasing the patient's agitation.

Lobotomy and Pain.

H. E. KING, J. CLAUSEN AND J. E. SCARFF (*The Journal of Nervous and Mental Disease*, August, 1950) describe a small series of unilateral lobotomies for intractable pain. In five of six cases the patients were relieved. The authors state that there is evidence that the peripheral pain threshold is not elevated but in fact is slightly lowered.

Evaluation of Electroconvulsive Therapy.

SHAFICA KARAGULLA (*The Journal of Mental Science*, October, 1950) states that from 1930 to 1948 he studied 923 patients treated in the Royal Edinburgh Hospital for mental and nervous disorders. He has attempted the long-term evaluation of electroconvulsive therapy. By statistical analysis he concludes that the percentage rate of discharge from hospital after a depressive illness does not vary greatly whether the patients are treated conservatively or by electroconvulsive therapy, and that the duration of stay in hospital does not seem to be reduced after electroconvulsive therapy. He comments that whatever the result of statistical comparison, clinical observation supports the therapeutic value of electroconvulsive therapy in the depressive states.

Wave Patterns in Epilepsy.

W. BARKER, S. BURGWIN AND D. J. SIMONS (*The Journal of Nervous and Mental Disease*, September, 1950) have recorded brain wave patterns of epileptic subjects during "Sodium Amytal" and ordinary interviews. They find that when there is blocking indicative of conflict associated with effort to recall and to communicate the experience, there is alteration in the wave pattern. In some cases the changes are sufficiently clear to indicate the significance of underlying psychological trauma. The authors conclude that convulsive symptoms may be produced by reactions within the central nervous system accompanying disintegration of the organism-environment relationship when distress within the integration rises to a critical level.

Iron Content of Cerebro-Spinal Fluid in Psychotic Conditions.

H. E. LEHMANN AND V. A. DRAL (*A.M.A. Archives of Neurology and Psychiatry*, March, 1951) stress the importance of iron metabolism in the central nervous system, especially the grey masses of the cerebrum and brainstem. They set out to examine the cerebro-spinal fluid of 98 patients suffering from various psychoses and to determine the relationship of cerebro-spinal fluid iron content to brain iron content. It was assumed that a low cerebro-spinal fluid iron content was indicative of increased brain metabolism and that high iron values reflected reduced cellular activity of the brain tissue. When the patients were divided into various diagnostic groups a statistically significant difference emerged between the cerebro-spinal fluid iron content of patients in the acute and deteriorated cases of schizophrenia; in the acute cases it was low and in the deteriorated cases it was high. In addition the difference between the cerebro-spinal fluid iron content of patients with organic psychoses and that of the group with acute schizophrenia was very significant, that is to say, in the authors' cases of general paralysis of the insane or parkinsonism the cerebro-spinal fluid iron content was raised.

War and Peace.

QUINCY WRIGHT (*The American Journal of Psychiatry*, September, 1950) discusses particular occasions of war, and asks why rivalries between States and international tensions should exist. He states that the answer is to be found less in the external grievances of a State than in the internal composition, conflicts, structure and policies of the super-community to which they belong. Tensions start in individual human minds; the more widely a social group expands, the more suppressed aggression exists and the more necessary it is to have an "out-group" to preserve the solidarity of the "in-group". States in close proximity, and today this may mean almost any State, will have some grievances against others. In a free society internal competition and rivalry allow for the discharge of aggression; this is not so with a rigid internal order. The author suggests that tensions and war might be reduced by a system of education, especially pre-school education, by a system of economics and politics in which insecurity was reduced, and by a system of harmless competition in politics, business or sport, and symbolically in art and literature. Such principles can apply both within one State and in a group of States.

Examination of the Complaining Witness in a Criminal Court.

LEO L. ORENSTEIN (*The American Journal of Psychiatry*, March, 1951) states that the focus of attention in a criminal court has been mainly directed towards the defendant with little attention to the complainant. Once legal procedure has commenced the accused is in a disadvantageous position, while to date the accuser has enjoyed immunity as well as sympathy. The psychiatrist in court is primarily to investigate the criminal and not the crime, but such comments would be more valuable were he able to evaluate the plaintiff as well. Three cases are quoted in which the accusers were children whose statements were established to be essentially fantasy based on individual psychopathology.

Delirium.

MAX LEVIN (*The American Journal of Psychiatry*, March, 1951) states that delirium is a psychosis characterized always by disorientation, and commonly by restlessness, dulness, fear, hallucinations and other mental symptoms. It is often, but not always, due to toxæmia, clearing up when the toxæmia has been corrected. It may also occur as a terminal event in the course of an organic dementia even when there has been no toxæmia; in such cases it may go on for months and years, and is irreversible. The disorientation of delirium differs in nature from that seen occasionally in paranoid schizophrenia. The delirious man, unlike the schizophrenic, tends to mistake the unfamiliar for the familiar (mistaking, for example, hospital for home, and nurse for wife). His thoughts and actions follow the patterns of lifelong habit. The difference is that the healthy man, with highest cerebral centres in good condition, is able to discern when a situation calls for a response out of the common groove. The delirious man, in contrast, has, from paralysis of the highest cerebral centres, lost this power of discrimination, and responds with habitual patterns of thought and action when they are no longer appropriate. With drug delirium it is advisable to discontinue the causative drug abruptly and completely. In the treatment of delirium it is unwise to use any drug that can itself cause delirium. Bromides and barbiturates are especially to be shunned; paraldehyde is the hypnotic recommended.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on July 26, 1951, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. K. C. T. RAWLE, the President, in the chair.

The Role of the Adrenal Cortex in Disease.

DR. KEITH S. HARRISON read a paper entitled "Role of the Adrenal Cortex in Disease" (see page 549).

DR. EMILY M. A. DAY read a paper on the pathological aspects of the adrenal cortex. This paper has not been made available for publication.

DR. J. K. MADDOX said that a completely new era in medicine was being entered. Selye's work was interesting and original. While no doubt many other workers had difficulty in accepting his views just as they were, Selye had given a tremendous stimulus. Many of his experimental results had been borne out, and had led to the testing by Hench and others in the clinical field of the substances under discussion; he had made a great contribution. Dr. Maddox referred to the value of the concise summaries presented by Dr. Harrison and Dr. Day, and said that they had saved the audience present at the meeting from the stress of reading the enormous literature now surrounding the subject.

DR. S. G. NELSON said that he had one question to ask the speakers. From time to time one was consulted by patients presenting not all the classical features of Addison's disease; but they were tired, thin, languid housewives. They had certain features in common—their blood pressure was low, they had symptoms of "nerves". On examining them, one found that they had been labouring under a good deal of stress. In private practice one hesitated to put them to the trouble of a great deal of investigation, as they did not present the classical features of Addison's disease; but they did respond dramatically to one of the forms of DOCA. Dr. Nelson asked whether such patients were suffering from chronic adrenal insufficiency, or whether the role of DOCA in their cure was merely symptomatic.

DR. W. J. MCCRISTAL congratulated Dr. Day and Dr. Harrison on the standard of their papers and on the manner in which they sifted experimentally proved evidence from assumption and conjecture. Dr. McCristal said that he would welcome Dr. Day and Dr. Harrison's comments on the reported work of Dr. Rose in Melbourne. He was aware that Dr. Sayers, of Utah, United States of America, had heralded the possible discovery of a neuro-humour acting through the hypothalamus and the effector cells of the adenohypophysis, and that adrenaline was one such factor that might be used in this connexion to provide a supply of corticotropic hormone for stimulation in turn of the adrenal cortex. Dr. McCristal said, nevertheless, that he was puzzled to know where a reported so-called powder entered into Dr. Rose's project.

DR. HALES WILSON asked Dr. Day a question about the test for adrenal cortical lack. He said that Professor D. M. Dunlop had recently stated that he considered the insulin sensitivity test one of the best. Dr. Wilson said that in a normal person, if one-tenth of a unit of insulin per kilogram of body weight was given intravenously and the blood sugar content estimated every half-hour, the result expressed graphically would be the inverse of a normal glucose tolerance curve. The same dose given in adrenal insufficiency would cause severe hypoglycæmia, so that only half the quantity should be used. The result in Addison's disease was like a diabetic glucose tolerance curve inverted. Dr. Wilson asked Dr. Day her opinion of this test.

Dr. Harrison, in reply, thanked Dr. Maddox for his words of appreciation. He said that the evaluation of Selye's studies remained for the future. His hypothesis was brilliant and stimulating, and might be correct. Dr. Harrison said that Dr. Nelson's patients presented a clinical problem. He thought that such cases of emotional exhaustion were very common, while Addison's disease was very rare. He doubted whether such people were subjected to sufficient stress, even at the present time, to exhaust their adrenal cortex. Stress, to do that, needed to be very gross and very prolonged. Those people could not be suffering from lack of adrenal cortical hormone; their response, if any, was due to pharmacological stimulation rather than to replacement. Dr. Harrison said that he did not know much about Rose's work. The work of many investigators had been directed to finding a stimulator of the pituitary. As yet no critical work had been published to indicate the identification of a neuro-humour. Adrenaline did stimulate the production of ACTH, but there was probably no evidence that it was a true neuro-humour. It was more a non-specific stimulating agent.

Dr. Day, in reply to Dr. McCristal, said that she thought it must be accepted until proved otherwise that something in the nature of a neuro-humour must exist, because if the stalk of the pituitary gland was severed from the central nervous system in such a way that there must be discontinuity between the neural element of the pituitary and the thalamus, and yet small venous plexuses and the circulation of the blood between the brain and the hypophysis were not interfered with, the function of the pituitary continued unchanged. There must be some way in which it could carry on that function quite apart from the central nervous system, otherwise it would atrophy and the results of such atrophy would appear. In reply to Dr. Hales Wilson, Dr. Day said that she had not used insulin sensitivity tests as Dr. Dunlop had suggested. She would not like to give insulin to anybody who she thought had Addison's disease, though perhaps a small dose with a good supply of glucose handy would be safe. The twenty-four hours' starvation test was an attempt to show the same thing. In these patients there must be depletion of the glycogen store, and to give insulin would easily cause hypoglycæmia.

Dr. Rawle, from the chair, thanked the speakers on behalf of the meeting for having tackled a difficult subject so well; they had cleared the air for many of those present.

A MEETING of the New South Wales Branch of the British Medical Association was held on May 31, 1951, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. K. C. T. RAWLE, the President, in the chair.

Emotional Factors in Allergy.

DR. D. M. ROSS read a paper entitled "Emotional Factors in Allergy" (see page 553).

DR. H. J. PRIOR read a paper entitled "Emotional Factors in Allergy" (see page 556).

DR. GUY LAWRANCE said that it was a long while since the subject had been discussed at a Branch meeting. A few months previously Professor Kennedy from England had given them his story of the anatomical basis of the emotions, and at the conclusion of his paper the professor of anatomy had asked where Professor Kennedy placed the anatomical centre for the emotions. Professor Kennedy could not say. Dr. Lawrance thought that it was possibly in the thalamus or lower down in the brain stem. Meduna, of shock fame and later of oxygen-carbon-dioxide therapy fame, held that the centres of the psychoneuroses were in the subcortical areas, the thalamus and further down along the brain stem. Recently at a meeting on the skin and psychosomatic skin manifestations, Dr. John Russell had said that he was fully conversant with the facts as outlined by the dermatologists. He fully accepted that the emotions, complexes and the like could go forth into the conscious in the form of conversion hysterias; he could not see any difficulty in the hypothesis that the repressed content might go out in a similar way and be recorded in the form of skin diseases. So it seemed that in allergies the emotion, aggression or dependence of the child would have some anatomical mode of expression whereby those parts of the anatomy involved in the production of allergy were connected with the emotions and were therefore the basic cause of the allergic symptom. That was as might be. Allergy was a dangerous topic. Dr. Frank Metzger, of America, a Fellow of the Society of Allergists and leader of the Psychosomatic Group there, said that when allergy existed it was necessary to treat and destroy the allergens. In many cases that could be accomplished. In many others it was noticed that, although the allergens were gone, the symptoms remained. In some cases the persistence of symptoms was due to infections (tonsils, kidney, gall-bladder *et cetera*). In that group the effects did not clear up. Another group in which the effects did not clear up was the group that had a mind—a mind not functioning satisfactorily; in them a psycho-neurotic or neurotic factor was at work. Dr. Lawrance referred to the case of a woman whom Dr. Metzger had treated for giant urticaria induced by the taking of aspirin. He cured that, but he wore a white coat while treating her. Afterwards, every time she saw him in a white coat, she burst out into hives. She did the same thing in the presence of clergymen

at the sight of their white collars. That was a clear case of psycho-neurotic attachment.

DR. R. S. STEEL stressed what Dr. Ross had mentioned—that it was very necessary to take a careful history and make a full physical examination, because, as he had said, there were many things that caused panting which were not allergic, and the condition was then not asthma. In general practice it was necessary to sort them out. There was, for example, bronchogenic carcinoma, even aortic aneurysm or syphilitic aortitis with regurgitation. Dr. Steel considered that psychogenic asthma was extremely rare. He recalled the history of a young boy, who sat at the table meal after meal eating his food rapidly—"bolting" his food. His parents, wanting to educate him, told him that he would choke and die if he did not eat more slowly. That was bad psychology. Such a young lad, not wanting to die, but wanting his food rapidly, started to breathe more quickly. The result was psychogenic asthma or hyperpnœa. Dr. Steel said that that was extremely rare in his experience. Dr. Prior had mentioned infection as a cause. Dr. Steel considered that probably all allergic manifestations had an organic basis. How was that? There was first heredity, which they knew according to statistics was involved in between 50% of cases (in the United States of America) and 80% of cases (in London); at the Royal Prince Alfred Hospital the figure was 68%. Infection also might play a part, and might cause physiological change in the epithelium or mucosa. How did that come about? There was the child born of allergic parents. Rarely allergic manifestations occurred under a few months. Then followed upper respiratory tract infection, damage to the mucosa, the absorption of inhalants, and then the typical manifestation, hay fever. The next time asthma occurred. It was interesting how frequently asthma followed measles or whooping-cough when there had been an infection or a history of hay fever and a mild respiratory tract disorder like mild bronchitis or "influenza". How did they account for eczema of endogenous origin and for urticaria? Damage to the mucosa of the bowel occurred through gastritis and enteritis *et cetera*. The question of light sensitivity had been raised. That could be brought on by taking quinine, by eating figs and so on. Those substances met the mucous membrane in the bowel and were absorbed; their absorption, whether or not their digestion was complete, was enough to produce manifestations in the shock tissue. Dr. Steel doubted whether there was any evidence to prove that any allergic condition was purely psychological in its foundation, but his opinion was still that psychogenic factors did influence the person suffering from an allergic manifestation. The position had been stated very well by Dr. Prior. Trouble at home, excitement, going to a wedding, anything of an emotional nature, was likely to bring on an attack of asthma, hay fever, migraine or hives. Over-tiredness was another factor, in that it allowed a fall of the blood pressure. Emotional factors played an important part in the production of attacks of urticaria, giant or macular. Dr. Steel thanked Dr. Ross for his classification, which had helped him considerably. Referring to the fourth group, those with personality defects, Dr. Steel said that they were the people with whom he had always failed. He had sent them to psychiatrists, but they had also failed. Such people figured in the books as invalid pensioners. Dr. Steel then referred to the problem presented by the child who reacted to discipline by attacks of asthma. The mother asked what she was to do; if she corrected the child, he had an attack of asthma; if she slapped him, the same thing occurred. Usually the mother was over-anxious. Sometimes the dependent child was not so manifest to the clinician until he had advanced to more adult years. Dr. Steel quoted the case of a man, aged thirty-one years, who had gone for examination with his mother; he was built like a boxer, but spoke and acted like a child. He was a dependent child at the age of thirty-one years. A number of workers in America were ceasing to carry out tests for food allergy, and he himself had for many years found it useless to give injections against foodstuffs.

DR. W. E. FISHER referred to observations made over the past four years on Australian ex-prisoners of war of the Japanese. Those men, as they came back to Australia, were in one sense a completely random sample. Although they had left Australia in batches from separate States, they had been shuffled and moved about in captivity to such an extent that for practical purposes an average group in one State was the same as the corresponding group in another. They had had the experiences of which all those present knew. Their health after their return was a matter for consideration. The Repatriation Commission had set up a committee in 1947 to consider the problems. About a year after the men returned, many of them were complaining of an ill-defined group of symptoms, comprising such features as loss of appetite in the morning, vomiting of breakfast, inability to eat without vomiting before nine or ten o'clock in the morning, undue fatigability towards the end of the day, unjustified irritability with their families at night, a certain amount of diarrhœa (the passage of three to five motions for one or more days every few days or weeks), sometimes pain of the hunger type of dyspepsia. Very little was found on ordinary investigation. The Repatriation Commission had it put up to them that the men were suffering from a new disease, not yet described. Dr. Fisher himself objected to that hypothesis as unsound. A glance through the files of the commission would show what had happened; the patients were investigated extensively and expensively and with sympathy, and no abnormality was found; then a certain proportion of medical advisers "skied the towel" and made a diagnosis of "anxiety state". That was not a good thing. Some government departments required access to such dossiers when the men applied for employment, and would then refuse to employ them. At first 10% of the ex-prisoners of war were surveyed, not very well. A survey of 100% was nearing completion, and it had been very well done. Out of the 6000 patients in New South Wales, at least one in three had been found to be harbouring hookworm or its cousin strongyloides. When that condition was treated, the patient's symptoms cleared up. The original diagnosis of anxiety state had not been justified. Of the patients, more than 90% would be found to have eosinophilia, and somewhere in the neighbourhood of 60% manifested urticaria, most commonly on the belt line or the buttocks—a very simple manifestation of allergy. That was an interesting example falling under Dr. Ross's first head; it showed that some allergic manifestations might be almost entirely somatic, and that one might err by trying to allow for more psychological factors. With regard to the importance of psychological factors in the other three categories, Dr. Prior had put his finger on the main question when he asked: "Which came first, the hen or the egg?"

A questioner asked whether Dr. Ross considered that the use of an antihistamine drug like "Hapamine" would be of any value in the treatment of the psychiatric symptoms. He remarked that he had used such treatment empirically, with what appeared to be some success.

DR. D. N. EVERINGHAM said that Dr. Ross's scheme had been helpful to many of those present. However, it was necessary to be cautious of pigeon-holing people. That might have the same serious consequences as Dr. Fisher had pointed out when the patient's condition had been labelled "anxiety state". When one spoke of a personality defect, the tendency was to lump it together with an intellectual defect as something irreversible. When one spoke of a person having an inborn defect, one was rather shelving the problem, assuming that not much could be done about it. Dr. Everingham thought that it was possible to guard against that attitude if it was remembered that just because the problem was difficult, because the patient did not seem to respond to treatment or to be trying to get rid of his disease, it did not follow that he had no reversible factor. There might be something organic present that made him a psychotic. He might have a psycho-neurotic condition which was not recognized. Dr. Everingham thought that while Dr. Ross's classification was used, in making it watertight one might be missing something in the organic field. If one could not handle the condition, then someone else might be able to do so. Used in that way the classification reached its right perspective.

DR. P. C. P. WAUGH asked Dr. Ross a question. He said that it had been assumed that the asthmatic attack was equivalent to a cry of rage or a cry for help. He wondered at what age period one could, by altering the basic factors, hope to achieve reasonable results by psychotherapy.

DR. BERNARD RILEY said that three points had appealed to him. The word "allergist" was a misnomer. The large group of allergic patients belonged to the physician. The allergist existed only because of the time factor—one could not be a psychiatrist, a dermatologist and an ear, nose and throat specialist. Dr. Riley had been pleased to hear Dr. Ross advocate the use of the term "allergic disorder" rather than "allergic disease". Dr. Riley believed that the conditions were not diseases. The majority of patients were extremely healthy in other ways. In addition to that, they had quite strong resistance to average infection. They were not diseases. He had also been interested in Dr. Prior's statement about giving the patients and their parents a reasonable explanation. Physicians should interview the children and their parents and should give the parents a simple explanation. They should explain that the children were really suffering from a defect in their defence—they were really vulnerable to things from outside such as foods and inhalants, and to things from inside such as mental stress and strain. They were extremely strong and healthy

children in other ways. Dr. Riley said that he was pleased that the two sections had come together; they were not closely connected enough, but they could not get on apart, and closer cooperation was needed among allergists, psychiatrists and psychologists. He hoped the cooperation would be as close as the antigen-antibody union.

Dr. Ross, in reply, said that he had no experience of antihistamine drugs in anxiety states. He had used adrenaline in increasing doses to try to relieve various somatic manifestations of anxiety. Referring to his classification, Dr. Ross said that he did not mean it to embrace four water-tight compartments. Each group shaded into the other. In so far as psychotherapy was concerned, the age of the patients was important, but something could be done for them at any age.

Dr. Prior, in reply, said that he felt obliged to explain that various more experienced and senior members of his specialty had turned down the presentation of a paper on the subject. Dr. Lawrance's comment that "this is deep and dangerous ground" cast light upon the problem. Reference had been made to the failure of psychiatrists to help very much in the bigger problems of allergic complications. Dr. Prior felt that, until they understood allergy, most psychiatrists would hesitate to be very dogmatic or to assume much responsibility in the handling of patients. It was the same with any conditions in which organic factors were involved. Dr. Prior said that he had had no experience of the value of environmental manipulation. Rogerson, at Guy's Hospital, who had done a great deal of work on the subject, apparently was reduced to sending many children to his convalescent home for varying periods, sometimes for years. Naturally one would hope to treat the child at home and adjust him to his home situation. That would in many cases be quite impossible without the help of social workers. Dr. Prior had been interested in Dr. Fisher's remarks, and hoped to see some of the work in print later on. He stressed that he did not think any psychiatrist would maintain that psychogenic factors were the main influence in allergy, or that they produced immunological allergy. But there were emotional and personality difficulties that cropped up, and allergists were left "holding the baby". If psychiatrists were to pull their weight, they must be more closely associated with the allergy clinic in the first instance.

Dr. Rawle, from the chair, thanked the speakers for their papers and those who had joined in the discussion. He referred to an incident mentioned by Sir Arthur Hurst in his book "Medical Essays". Sir Arthur Hurst, on visiting a certain town in England, always used to suffer an attack of asthma. He came to the conclusion that the cause must be psychological, and decided to spend a week-end there and not have an attack of asthma; he succeeded. Dr. Rawle said that he had seen one form of migraine much relieved by the administration of "Hapamine", which did seem to give relief, but it did not cure the patient.

THE annual general meeting of the Special Group on Aviation Medicine was held on June 14, 1951, at 49 Mathoura Road, Toorak, Melbourne, AIR COMMODORE E. A. DALEY in the chair. A number of resolutions were adopted to assist in the formation of the group. New office-bearers and new members were elected.

Recent Overseas Trends in Aviation Medicine.

AIR COMMODORE E. A. DALEY, discussing recent overseas trends in aviation medicine, indicated that the evolution of the jet engine had created aircraft whose speed, rate of climb and attainable heights had created entirely new physiological problems in maintaining aircrews and passengers in this new environment. Matters of medical interest involved two aspects: (i) the medical problems of high altitude, and (ii) the medical problems of high speed.

On the subject of medical problems of high altitude, Air Commodore Daley referred to the means of maintaining man at high altitudes involving the use of supplementary oxygen, pressure waistcoats, pressure suits and pressure cabins, the last of which was receiving greater consideration at present. Associated with pressurized cabins was the problem of explosive decompression when from structural failure or enemy cannon shell pressurization was destroyed almost instantaneously, producing the physiological problems of sudden ascent from, say, 20,000 to 45,000 feet. Other matters connected with high altitude were those affecting visual perception, cockpit illumination and glare at altitudes requiring suitable visual protection for the pilot. Next was the greenhouse effect of the sun's rays through the "Perspex" canopy, and lastly was the possible effect of cosmic rays—results of experiments carried out by the Americans seemed to indicate that these might present a biological problem.

Discussing high speed, Air Commodore Daley referred to the fundamental question of sonic and ultrasonic "sound", these being associated with the running of jet aircraft not only in the air but on the ground. Suitable protection of the ears appeared to be sufficient, and no major effects were proved to exist as a result of subjection to these frequencies; intensity rather than the frequency had the most effect.

Next Air Commodore Daley raised the question of escape from aircraft travelling at those high speeds and mentioned the ejection seat which the pilot could use at will in emergency; it precipitated him out through the top of the aircraft with suitable protection and parachute facilities. Air Commodore Daley also referred to the fact that high speed produced heating of the aircraft and special consideration was required with regard to ventilation and cooling of the cabins and cockpit. The use of backward-facing seats, so that personnel could take impact over a wide area in the event of a crash, was stressed by him as being an accepted principle.

The question of supersonics was referred to and the relationship indicated between the speed of aircraft and that of sound. Air Commodore Daley said that that was producing new problems for the pilot, in that the airflow changed over aircraft as the speed of sound was approached, and certain specific alterations occurred which he had to interpret and allow for. The passage from the sonic through the transsonic barrier to the supersonic would appear to be well within man's grasp.

Air Commodore Daley also mentioned the question of "cybernetics"—the study of human control functions and the mechanical, electrical and chemical systems designed to replace them. He said that with increase in speed man's reaction time was becoming a weak link in the chain of events, and whilst it did not appear that physical standards were being raised in the selection of pilots and navigators *et cetera*, it was suggested that some greater heed might be paid to reaction time and ability to interpret and quickly use instruments. It might be that man would get further back in the chain of events and would use the mechanical, electrical and chemical aid, for example, as radar was used as vision, and be the one who would be a controller of the devices rather than the person who activated the controls.

In closing, Air Commodore Daley indicated that developments had brought the aeronautical engineer and the aviation medicine worker closer and closer together, and the latter was in the forefront of developments along with his technical colleagues.

Recent Trends in Civil Aviation in Europe.

DR. E. H. ANDERSON spoke on recent trends in civil aviation in Europe. He described the exhibits seen at the Society of British Aircraft Constructors' display at Farnborough in September, 1950. The predominant features of the aircraft displayed were the change-over from piston engines to turbines and jet propulsion, and the almost universal use of cabin pressurization in passenger aircraft; only small feeder line aircraft were not pressurized. A steady improvement was found in crew compartment design, particularly in instrument layout and control identification. Passenger cabins were roomier, and seats more comfortable. Larger windows and better visibility were welcome features. Commercial aircraft in the news at present, such as the Brabazon, the Comet, the Viscount, the Hermes and the Ambassador, were described, and an attempt was made to give an idea of the spectacular flying performances of some of those aircraft.

Dr. Anderson went on to discuss the question of backward-facing seats in passenger aircraft. He said that forces of up to 57 times their own weight had been withstood successfully by persons seated in that position in properly stressed seats. Medical officers in Europe were unanimous in their opinion that greater protection was afforded in that way, and wondered why the idea had not been introduced generally into civil aviation. The idea that people would not like it seemed to be unjustified by Transport Command reports. The reason that the idea had not so far been put into production seemed to be the unwillingness of any airline operator to make the first move. The objections seemed to be that to introduce the system would awaken in passengers' minds the possibility of accident and that a certain proportion of passengers would not like it. Operators were naturally unwilling to do anything which in their view would weaken passenger appeal. The most favoured suggestion was that the controlling authority in each country

should regulate for introduction of the principle in all new aircraft. A striking example was given by Dr. Anderson of the protection afforded by backward-facing seats. In December, 1950, a Hastings aircraft fitted with backward-facing seats stressed to 20G had crashed near Benghazi, and although all five of the crew were killed (all were facing forwards), all the passengers escaped without serious injury, despite the fact that all the engines broke away from their mountings, one wing was torn off and the aircraft finally turned a complete somersault.

Another question discussed by Dr. Anderson was the need for providing emergency oxygen equipment in high altitude aircraft. The problem arose from the possibility of a sudden major loss of pressure in a pressurized cabin at high altitude, for example, 40,000 feet. The dangers of that explosive decompression, as it was called, made it necessary, in the opinion of medical officers, to provide emergency oxygen equipment in the aircraft concerned until it had been shown by experience in actual operations that such a thing would not happen. The precaution was thought necessary because experiments had shown that at 40,000 feet a healthy subject at rest had only about twenty seconds in which to do something effective and had only three to five minutes to live. As far as crew members were concerned, they could be presumed to be physically fit and would react immediately and successfully if supplemental oxygen was available. Passengers, however, were not all physically fit, and the effects on them of high degrees of oxygen lack would be disastrous unless oxygen was avilable and a capable person was available to administer it. Another factor was that, having survived the immediate danger with the descent of the aircraft to moderate altitudes, passengers might be exposed to further peril from oxygen lack by the necessity of the aircraft to fly at a higher altitude again in order to reach a landing point. That situation was caused by the fact that jet engines used fuel at an excessive rate at lower altitudes. It was for those reasons that medical officers had been strongly advising the installation of emergency oxygen equipment in the aircraft concerned at least for an interim proving period.

A MEETING of the New South Wales Branch of the British Medical Association was held at Saint Vincent's Hospital, Darlinghurst, on July 19, 1951. The meeting took the form of a series of clinical demonstrations by members of the honorary medical and surgical staff of the hospital.

Lymphangioma.

DR. V. J. KINSELLA showed a young woman, aged twenty years, who had suffered a road accident sixteen years previously in Scotland; this had led to an operation in the left flank, at which a tumour was found. She had been well till six months before the meeting when small, raised, scaling, red papules, some of them vesicular, appeared around the wound. Biopsy of one of the lesions revealed lymphangioma. A letter written to Scotland, inquiring about the nature of the tumour revealed sixteen years previously, brought the reply, "lymphangioma". The patient was treated by radiotherapy. Dr. Kinsella said that it was too early to assess results.

Non-Specific Ulcerative Colitis.

Dr. Kinsella then showed specimens of colon representing different types of colon disease: (i) the thick, stiff "lead pipe"; (ii) the soft "granulation-tissue colon" set in a great mass of thick, stiff, chronically inflamed pericolic fat and mesentery; (iii) the type with conspicuous, numerous, pedunculated pseudopolypi. These were from patients who had been treated by complete colectomy, after the physician (Dr. Bruce Hall) had concluded that medical treatment would not succeed. In all three cases (as in three others) the results had been very good. One patient, not yet discharged from hospital, was shown at the meeting.

Pyloric Lesions.

Dr. Kinsella concluded with a discussion of pyloric lesions, illustrated by skiagrams. The lesions included hyperplastic gastritis, follicular gastritis, marginal pyloric erosions, adhesions (due to gall-bladder disease, to previous cholecystectomy, and to previous transverse colectomy), "pyloric piles", hypertrophic stenosis of the pylorus (with and without gastritis and gastric ulcer), penetrating peptic ulcer in the pyloric region, penetrating ulcer at some distance from the pylorus causing secondary pyloric obstruction, and "tobacco-pouch" stomach in various stages.

Neurofibromatosis: Plexiform Neuroma: Mediastinal Tumour.

DR. J. E. SHERWOOD presented a man, aged twenty-nine years, who when first examined complained of pain across his chest, with a feeling of pressure there, for three months. He stated also that he had two cysts on his back. His only significant previous illness was bronchial asthma. He stated that his grandmother (on his mother's side) had a "nodulated" condition of her skin. His mother had had the same condition always, with a lump on the volar aspect of the right wrist. He himself had a similar skin condition and a similar lump on the volar aspect of the right wrist. On examination the patient was found to weigh nine stone two pounds. His colour and nutrition were fairly good. He had the diffuse pigmentary skin changes with *"café au lait"* patches characteristic of neurofibromatosis. The changes were affecting chiefly the skin of the abdomen and trunk. Occasional small fibromata were noticeable on the trunk. He appeared also to have tender neurofibromata in the region of the left elbow joint and a linear collection of them extending along the volar aspect of the left forearm in the line of the median nerve trunk. In addition he had a diffuse swelling over the volar aspect of the right wrist, which was extremely sensitive to palpation and was probably a plexiform neuroma. Finally, X-ray examination of the chest revealed a mediastinal tumour, clearly seen in antero-posterior and lateral views. The heart, lungs and blood pressure appeared to be normal. The blood pressure was 120 millimetres of mercury, systolic, and 80 millimetres, diastolic, in both arms. No clinical signs of aortic aneurysm were present. The abdomen, apart from the skin changes, appeared normal. No further neurological abnormality could be detected. The urine was neutral in reaction, with a specific gravity of 1020 and no albumin or sugar present. A Casoni test and a blood Wassermann test yielded negative results. A blood count revealed 5,470,000 erythrocytes per cubic millimetre, a hæmoglobin value of 110% (16·0 grammes *per centum*), a colour index of 1·0, and a total leucocyte count of 8000 per cubic millimetre made up of neutrophile cells 67%, eosinophile cells 5%, monocytes 24%, lymphocytes 24% and band forms 1%. X-ray examination showed a dense round mass in the upper part of the mediastinum on the left side, lying anterior to the aorta and trachea. The trachea was displaced slightly to the right. There was no displacement of the aorta. The lower end of the right radius was deformed, and there was a hollowing out of the cortical bone on its radial aspect. There was some irregularity of the radial styloid and distal end of the radius. No evidence of decalcification was seen. All the changes were in relation to the large soft-tissue swelling throughout the wrist. Dr. Sherwood said that points of interest about the case were the appearance of typical neurofibromatosis, the well-developed plexiform neuroma, the accompanying skeletal changes, the probable neuromatous mediastinal tumour, and the familial history. The patient's mother had been found to have evidence of generalized neurofibromatosis with a well-developed plexiform neuroma in the same situation as her son's.

"Glandular Fever" Presenting as Aseptic Meningitis.

Dr. Sherwood's next patient was a boy, aged fourteen years, who had been well until June 19, 1951, when he awoke complaining of frontal headache. The headache rapidly increased in severity and became associated with nausea and vomiting. It was relieved by lumbar puncture on June 20, when the patient was an out-patient. Lumbar puncture was repeated on June 21, after which the patient was admitted to hospital.

On his admission to hospital the patient appeared drowsy and ill, lying curled up on his left side in bed; photophobia was noticeable. His temperature was 100·8° F., his pulse rate was 100 per minute and his respirations numbered 20 per minute. Neck rigidity was present and Kernig's sign was elicited. His pupils were equal and reacted to light and accommodation. The knee jerks were active and the plantar reflexes were flexor in type. His blood pressure was 140 millimetres of mercury, systolic, and 100 millimetres, diastolic. The urine was clear. Examination of the heart showed that the apex beat was in the fifth left intercostal space three and a half inches from the middle line; the sounds were normal. The lungs and abdomen appeared free of abnormality. There was evidence of mild *otitis media*. A provisional diagnosis of meningitis was made.

Next day icterus was noticeable, chiefly in the scleræ; there was also an evanescent erythematous rash affecting the trunk, arms and legs. Later the jaundice progressively increased, and the stools became lighter and the urine darker. Enlarged lymph glands were noticeable in the

posterior triangles of the neck, the axillæ and the groins. The treatment consisted of penicillin given parenterally and sulphadiazine given orally.

Dr. Sherwood said that the boy's general improvement had been rapid. The meningitic signs, glandular enlargement and jaundice cleared in the order stated over a period of twenty days. At the time of the meeting he was comparatively well. During the course of the illness a number of investigations were carried out. On June 22 a full blood count showed that the erythrocytes numbered 4,930,000 per cubic millimetre and the hæmoglobin value was 98%; the leucocytes numbered 6300 per cubic millimetre, 68% being neutrophile cells, 27% lymphocytes, 4% mononuclear cells and 1% eosinophile cells. A throat swab yielded a scanty growth of hæmolytic streptococci. An X-ray examination of the chest and the cervical part of the spine revealed no abnormality. On June 23 the cerebro-spinal fluid was found to be blood-stained; it contained 9000 erythrocytes per cubic millimetre, and eight polymorphonuclear leucocytes and 18 lymphocytes per cubic millimetre. On June 27 liver function tests gave the following results. Urobilinogen was absent from the urine. The serum bilirubin content was 4·1 grammes *per centum*, the serum alkaline phosphatase content was 24 King-Armstrong units, the colloidal gold flocculation test produced an incomplete positive reaction, the thymol flocculation test produced a strongly positive reaction and the zinc sulphate turbidity test produced a figure of 16·0 units. A full blood count showed that the leucocytes numbered 7000 per cubic millimetre, 50% being neutrophile cells, 41% lymphocytes, 3% mononuclear cells and 6% eosinophile cells. Typical glandular fever cells were present. On June 28 the Paul-Bunnell test produced a negative result. On July 4 the leucocytes numbered 6700 per cubic millimetre, 55% being neutrophile cells, 34% lymphocytes, 7% mononuclear cells and 4% eosinophile cells. Occasional glandular fever cells were present.

Dr. Sherwood said that although the diagnosis of "glandular fever" (infectious mononucleosis) had been made, it was realized that, apart from the initial slight leucopenia and the later finding of "glandular fever cells", such a diagnosis on the blood findings had little to recommend it. On the other hand, the extent of the lymph gland enlargement and the evanescent rash seemed to favour it clinically, and seemed to suggest that the hepatitis accompanied the glandular fever rather than being the primary cause of the illness. The negative response to the Paul-Bunnell test did not appear to be of any great significance, although a positive finding would have been helpful.

A MEETING of the Victorian Branch of the British Medical Association was held in the Department of Pathology, University of Melbourne, on August 15, 1951. The meeting took the form of a series of demonstrations presented by lecturers, demonstrators and research workers in the department, and subjects chosen were such as were of special interest to the individuals concerned.

DR. S. J. BAKER illustrated some anæmias of infancy and childhood with photomicrographs and coloured lantern slides, which were demonstrated on a screen. These illustrations were of blood corpuscles of various types which are seen in the various anæmias of children. A general review of these anæmias was given, the material being used as the text.

DR. DORA BIALESTOCK reviewed the work that she had been doing for the last two years on the investigation of nephritis. Using collodion particles as the indicator, she had shown that these may be changed, when mixed with an extract of kidney substance, in such a way that they were precipitated by a serum from a patient with nephritis, but not by a serum from a normal patient.

DR. J. L. BIGNELL demonstrated papilloedema and optic atrophy by means of drawings of the ophthalmoscopic appearances of the fundi and photomicrographs of sections made of the posterior part of the eye including the area of the optic disk. A wide range of conditions was illustrated.

DR. D. C. COWLING gave an account of cases of *polyarteritis nodosa* encountered recently at the Royal Melbourne Hospital. This was illustrated by photomicrographs taken from a larger series.

DR. G. S. CHRISTIE demonstrated neoplasms of the thymus. He showed 19 specimens of tumours of the thymus, and these included the various kinds of malignant growth. Some cystic tumours or tumours with associated cysts were included.

DR. J. A. FORBES demonstrated radioautography with radioactive iodine. He showed specimens of transplantable rat thyreoid tumours and some human thyreoid material from patients who had received radioactive iodine. The distribution of the iodine in such tissue was shown, and this was compared with the sections of the same gland. The variability in the "take up" of iodine in these conditions was clearly demonstrated. Specimens of rats containing tumours were included in the demonstration, and a Geiger counter was shown.

DR. J. F. FUNDER and DR. S. F. REID discussed regional ileitis (Crohn's disease). The general macroscopic features of the condition were illustrated, and photomicrographs were presented showing the characteristic histological structure. The relation of the pathological features to the treatment of the condition was discussed.

DR. D. R. GAULD demonstrated cystic disease of the lung with examples of almost all kinds of cysts of the lung. There was a good series of X-ray films showing the appearances of these conditions during life.

DR. R. A. HAYES discussed malignant lymphoma. By means of a series of photomicrographs and lantern slides projected on a screen, he showed examples of follicular lymphoma, leuchæmia, Hodgkin's disease and lymphosarcoma.

DR. I. C. HEINZ demonstrated acute pancreatitis with a good series of macroscopic specimens of the condition in various stages and degrees and some photomicrographs. The ætiology of the condition was discussed.

DR. J. D. HICKS discussed hyperplasia of the thymus. He showed a considerable number of examples of the condition and discussed its relation to *myasthenia gravis*. The histological changes found in the thymus and the development of cysts in the organ were also considered.

DR. J. T. HUESTON demonstrated hyperplasia of the breast with photographs and photomicrographs of characteristic examples of various degrees and kinds of hyperplasia.

DR. F. X. G. HURLEY gave an extensive demonstration of arteriosclerosis. He presented the various clinical and experimental observations which bear on the subject and discussed the hypotheses of origin of the condition.

DR. E. S. R. HUGHES illustrated rectal tumours by means of actual specimens, almost every variety of carcinoma of this organ being included amongst the types presented. The general features of the disease and their relation to its surgical treatment were discussed.

DR. W. E. KING presented a study of thyreoid disease with radioactive iodine.

MR. N. MCCALLUM discussed the toxicology of the barbiturates and showed the great advances that had been made recently, not only in the direction of determining accurately the amounts of barbiturates present in a tissue, but also in the recognition of different types of these drugs.

MISS D. MOUNTFORD demonstrated methods of determining antibody titre.

DR. J. S. PETERS discussed renal calculi. The various factors responsible for the development of stone and the general ætiology of the condition were discussed. The results of experimental work in rats were also presented.

DR. A. W. POUND demonstrated experimental work in tuberculosis. He explained that chemical fractionation of tubercle bacilli gave substances which had demonstrably different effects on the tissues as shown by their use as antigens in titration of sera from persons with tuberculosis.

DR. BRUCE ROBINSON discussed peptic ulcers. A general review with illustrations including particularly drawings, graphs and photomicrographs was presented.

DR. I. O. STAHLE presented benign tumours of the dermis. These included neurofibroma, dermatofibroma, leiomyoma, glomus tumour and xanthoma.

DR. G. B. WESTMORE reviewed Paget's disease of bone. The review was illustrated with macroscopic specimens, photographs and photomicrographs.

DR. A. L. WILLIAMS presented a demonstration of coronary occlusive disease in children. The material consisted of specimens from a series of cases recently encountered at the Children's Hospital. These included examples from a number of conditions in which the cardio-vascular system is specially involved, such as rheumatic fever, *polyarteritis nodosa* and the like.

MR. J. GUTHRIE gave a demonstration of apparatus, including the histokine, the Fanz knife sharpener, photomicrographic apparatus (Panphot) and microtomes.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

MEETING OF A MEDICAL BOARD.[1]

[*Sydney Gazette*, July 29, 1820.]

Government House,
Sydney,
29th July, 1820.

A medical Board consisting of the following surgeons: viz.—

J. M. BRYDONE, Esq., Surgeon R.N.,
G. A. STEPHENSON, Esq., Surgeon 48th Regt., and
JAMES HUNTER, Surgeon R.N.

Wherefore J. M. BRYDONE was President, having lately been appointed by his Excellency the Governor to enquire into and report on certain Subjects connected with the Professional Practice here: and among other Things to examine and report on the Qualifications of certain Persons who were represented as practicing Surgery and Physic within the territory of New South Wales and more especially at Sydney, and believed to be exercising such Art and Profession to the Prejudice of the Ignorant and Unwary who have placed themselves under their medical charge—

And the Board having called before them and examined
Thomas LAWSON
George WHITE
John BRENNAN
Joseph HYAMS and
Simeon LEAR

who were known to be exercising the Practice of Surgery and Medicine, has reported to his Excellency that the said Persons are not duly qualified to practise either as Surgeons or Physicians, being ignorant of those Professions.

His Excellency the Governor is hereon pleased to order and direct that the said Persons: namely
Thomas LAWSON,
George WHITE
John BRENNAN
Joseph HYAMS and
Simeon LEAR

do forthwith cease to practice either as Surgeons or Physicians at Sydney or in any part of the Territory of New South Wales, on Pain of being prosecuted for the same with the utmost Rigour of the Law.

By His Excellency's Command,

J. J. CAMPBELL, Secretary.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

PANCREATITIS AT THE ROYAL NORTH SHORE HOSPITAL OF SYDNEY.

SIR: Dr. Thomas F. Rose's scholarly paper (THE MEDICAL JOURNAL OF AUSTRALIA, October 6, 1951, page 453) recalls to mind two cases of long ago.

When I joined the staff of the hospital in 1909 I made a post-mortem examination of a middle-aged man who had suffered an obscure abdominal illness. I well remember the interest of two senior surgeons at the demonstration of small, scattered patches of fat necrosis in the omentum and mesentery, and of a swollen pancreas mottled with blood.

The second striking case, twenty years later, should come within the period in Dr. Rose's list. It was that of a nurse who complained of paroxysms of agonizing pain and was at first said to be malingering: she did well without operation, but returned unduly early to duty and relapsed. Fortunately

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED SEPTEMBER 29, 1951.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	..	..	..	..	..	..	..	..	..
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	..	..	..	..	..	..	..
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	1(1)	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	..	..	13(10)	..	..	1	6	..	20
Diphtheria	7(4)	..	7(5)	..	3(2)	..	..	..	17
Dysentery (Bacillary)	..	..	1(1)	..	2(1)	..	..	..	3
Encephalitis	9(3)	..	..	..	..	1	..	..	10
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	..	..	..	..	12(8)	..	..	..	12
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	1	..	..	..	..	..	1
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	2(2)	1	..	..	1(1)	3(2)	..	..	7
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	1	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	4(1)	4(2)	45(32)	2	..	..	..	55
Puerperal Fever	..	..	..	..	..	1	..	..	1
Rubella	..	10(5)	2(2)	..	3(2)	..	..	..	15
Salmonella Infection	..	..	..	..	..	..	..	..	..
Scarlet Fever	21(7)	3(3)	3(2)	2(1)	4(1)	8(6)	..	..	41
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	..	..	..	..	..
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	29(26)	6(2)	14(10)	8(4)	11(10)	7(2)	1	..	76
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

the ultimate result was good and she continued her career. In 1950 she was a ward sister in another hospital.

Yours, etc.,

GUY GRIFFITHS.

131 Macquarie Street,
Sydney,
October 12, 1951.

MEDICAL HISTORY OF THE WAR 1939–1945.

SIR: I should be glad if you would allow me space to notify my colleagues that the second volume of the Medical War History has been completed in draft and should be ready for the printer early next year. This volume deals with campaigns and other experiences of the Australian Imperial Force in the Middle East and the Far East. I wish also to make an appeal to those who possess photographs covering this period. A number of medical officers have already helped me in this way and I should be very glad if any others who can help would let me know.

The first volume is now in the hands of the printer, and it is hoped that it will be published next year.

Yours, etc.,

ALLAN S. WALKER,
Medical War Historian.

Department of the Interior,
Canberra,
October 10, 1951.

Obituary.

WILFRID WANOSTROCHT GIBLIN.

WE regret to announce the death of Dr. Wilfrid Wanostrocht Giblin, which occurred on October 10, 1951, at Hobart, Tasmania.

MAY HANNAH HARRIS.

WE regret to announce the death of Dr. May Hannah Harris, which occurred on October 16, 1951, at Newcastle, New South Wales.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Lane, Margery Ritchie, M.B., B.S., 1951 (Univ. Sydney), "Claverton", Alma Street, Pymble.

Garner, Ralph Lindsay, M.B., B.S., 1951 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

The undermentioned have been elected members of the New South Wales Branch of the British Medical Association:

Bannon, Paul Edward, M.B., B.S., 1951 (Univ. Sydney), 4 Cabramatta Road, Mosman.

Burns, Robert John, M.B., B.S., 1950 (Univ. Sydney), Women's Hospital, Crown Street, Sydney.

Carrick, Denise Myles, M.B., B.S., 1951 (Univ. Sydney), 2 Merlin Street, Roseville.

Cope, Thomas Ian, M.B., B.S., 1950 (Univ. Sydney), 66 Wallis Avenue, Strathfield.

Dickson, John Grant, M.B., B.S., 1944 (Univ. Sydney), 7 Victoria Street, Strathfield.

Drummond, John McPherson, M.B., B.S., 1951 (Univ. Sydney), 21 Alexandra Street, Hunters Hill.

Fenwick, Louis, M.B., B.S., 1950 (Univ. Sydney), Sydney Hospital, Sydney.

Ferguson, Edward Stephen Perry, M.B., B.S., 1950 (Univ. Sydney), 20 Beach Road, Collaroy.

Findlay, Wilmet Helena, M.B., B.S., 1951 (Univ. Sydney), Rachel Forster Hospital for Women and Children, Redfern.

Ireland, Basil John, M.B., B.S., 1950 (Univ. Sydney), Saint Vincent's Hospital, Darlinghurst.

Leeser, Felix, registered in accordance with the provisions of Section 17B of the *Medical Practitioners Act*, 1938-1945, 243 Elizabeth Street, Sydney.

Leitch, David Stanley, M.B., B.S., 1950 (Univ. Sydney), "Springville", Narrabri.

Ming, Edna Gork, M.B., B.S., 1942 (Univ. Sydney), Highview Avenue, Manly Vale.

The undermentioned have been elected members of the South Australian Branch of the British Medical Association:

Anderson, Albert Raymond, M.B., B.S., 1951 (Univ. Adelaide), 261 Magill Road, Trinity Gardens.

Cawte, John Ewart, M.B., B.S., 1949 (Univ. Adelaide), Northfield Mental Hospital, Northfield.

Milne, Kevin Fowler, M.B., B.S., 1951 (Univ. Adelaide), 6 Elston Street, Lockleys.

Diary for the Month.

Nov. 1.—South Australian Branch, B.M.A.: Council Meeting.
Nov. 2.—Queensland Branch, B.M.A.: Branch Meeting.
Nov. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
Nov. 7.—Western Australian Branch, B.M.A.: Council Meeting.
Nov. 9.—Queensland Branch, B.M.A.: Council Meeting.
Nov. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

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